EXHIBIT III.5

Expert Report of Matthew Perri III, BS Pharm, PhD, RPh

March 25, 2019

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INTRODUCTION

1. I was retained on behalf of Plaintiffs to evaluate the record and ascertain the significance, if any, of Defendants' activities from a marketing perspective. Specifically, I was tasked with evaluation of Defendants' marketing of prescription opioids. This Report provides a detailed summary of my findings.

QUALIFICATIONS

2. My name is Matthew Perri III. I am a Professor at the University of Georgia. I received my Bachelor of Science in Pharmacy from Temple University in Philadelphia, Pennsylvania in 1981. In 1985, I obtained my Doctor of Philosophy, with a dual concentration in Pharmacy and Marketing, from the University of South Carolina. I have held academic and administrative positions at the University of Georgia, College of Pharmacy, since 1985.

3. My current title is Professor and Associate Head of the Department of Clinical and Administrative Pharmacy at the College of Pharmacy. I am a member of the University's Graduate Faculty and Adjunct Faculty of Gerontology in the College of Public Health. I also serve as the Director of the Pharm D / MBA dual degree program, and I am an invited member of the University of Georgia Teaching Academy where the University's best teachers are recognized for their contributions to education.

4. At the University of Georgia, I teach graduate and undergraduate courses in health care and pharmaceutical marketing, management, research methods, patient communications, patient care skills laboratories, and biomedical statistics. Some of these courses attract students from the School of Public Health, the Terry College of Business, and the College of Education.

5. I have published articles in peer-reviewed journals such as Medical Care, Journal of Health Care Marketing, Health Marketing Quarterly, Value in Health, and the Journal of Health Communication. I have served as a peer-review referee for more than two dozen academic journals such as the Journal of Advertising, Clinical Therapeutics, Health Marketing Quarterly, the Journal of Health Care Marketing and Management, and Medical Care. I have also published

articles written for health care professionals in professional publications such as Pharmaceutical Executive, Southern Medical Journal, Drug Store News, and The Consultant Pharmacist.

6. I have made numerous presentations to audiences including academicians, researchers, industry professionals, policy makers, healthcare professionals, civic organizations, and consumer groups. Many of these were peer-reviewed or invited presentations. Recently, I was the invited keynote speaker at the Emory School of Medicine conference on Geriatrics where I spoke on strategies to help physicians understand pharmaceutical marketing.

7. I have authored two books, Pharmaceutical Marketing and Financial Analysis in Pharmacy Practice, as well as book chapters, and monographs on topics related to marketing, management, and clinical pharmacy care.

8. I have conducted extensive original research as principal, co-investigator, or consultant related to pharmaceutical marketing and related policy analyses, including work in the area of opioids funded by private and public sources, such as the National Institutes of Health the Substance Abuse and Mental Health Services Administration, private foundations, and State and Federal Government.

9. My current research includes two, multi-year grants from the National Institutes of Health (NIH) and the Substance Abuse and Mental Health Services Administration (SAMHSA). The NIH grant investigates the effects of Medicaid prescription drug benefit program policy changes on patient outcomes, including death, in the Medicaid population. The SAMHSA grant is a training project which aims to provide skills to pharmacists, social workers, psychologists, and other health professionals to proactively recognize patients who may be at higher risk for health problems due to substance abuse.[1]

[1] Opioid Prescribing in Medicaid: Healthcare Utilization and Deaths from Overdose. Grant No: 1R01DA039930-01A1 2016-2019; $675,000 National Institutes of Health (NIDA), Principle Investigator. UGA SBIRT Inter-professional Training Program, Grant No: 1H79T1026457-01, 2016-2019; $851,016 Department of Health and Human Services, Co-Investigator.

10. I have been involved with various non-paid national and state service and consulting activities including, for example, my longstanding work with Georgia Medicaid,[2] service on the Boards of the Association for Marketing and Health Care Research and the Medical College of Georgia / Blue Cross Blue Shield Center for Healthcare Improvement, and service as a consultant to the Georgia Senate Committee on Cost Controls in State Funded Health Plans. I have been an invited participant to the National Consumers League workshop on direct-to-consumer prescription drug advertising, and to the Agency for Healthcare Research and Quality/U.S. Food and Drug Administration "Think Tank" on current issues and future research agenda for the marketing and advertising of prescription medications.

11. I have also been a paid marketing consultant to organizations, including hospitals and long-term care facilities, independent marketing research companies, pharmacy organizations, pharmaceutical companies, and chain and independent pharmacies. My consulting activities have also included work with the U.S. Department of Justice, State Attorneys General, and private attorneys in litigation related to the marketing of pharmaceutical products.

12. Prior to becoming a registered pharmacist, I worked as a pharmaceutical sales representative for a multinational pharmaceutical company.[3] I have been a registered pharmacist since 1981 and am currently licensed to practice pharmacy in Georgia and South Carolina. Since 2002, I have served as a part-time volunteer pharmacist at the Mercy Health Center, an independent, not-for-profit, comprehensive health center.

[2] I was a Board member (2001-2012) and Chair (2004-2010) of the Georgia Department of Community Health, Drug Utilization Review Board (DURB). I was reappointed to the DURB in October of 2018. The DURB, composed of pharmacists, prescribers, insurers, and patient advocates, is responsible for recommending the drugs listed on the State's preferred drug list for all State-funded health plans.

[3] In 1979 and 1980, I was a Pharmacy Student Sales Representative (PSSR) for the Dome Division of Miles Laboratories. In this position, I was trained and detailed a line of dermatological products to dermatologists, obstetricians, gynecologists, and general practitioners. Pharmacy distribution was also an important aspect of this position due to planned new product introductions and initial stocking needs. The PSSR program was a work-coop program, approved by Temple University School of Pharmacy and sponsored by Miles Pharmaceuticals.

METHODOLOGY

13. In my analysis of this case, I applied my education, training, and experience in teaching, research, consulting, and clinical pharmacy to formulate my opinions. My perspectives on pharmaceutical marketing are based on my marketing education and work in pharmaceutical marketing, including research, writing and publishing, consulting, teaching, and training of doctoral level graduate students, many of whom currently work in the pharmaceutical industry. I have subjected my research and conclusions regarding marketing issues to peer-review on numerous occasions.

14. I applied generally accepted principles of marketing, when I evaluated Defendants' internal marketing environment, the marketing mix variables (price, place, product, and promotion), and Defendants' marketing segmentation, targeting, and positioning strategies and tactics. Using this framework, I identified marketing behaviors and assessed the significance of these behaviors.

15. Case study methods, grounded in marketing principles, were used to systematically assemble and articulate information (data collection, analysis and interpretation[4]) related to Defendants' marketing activities. These methods are used and relied upon by experts in my field. In the present context, this case study is an in-depth, empirical inquiry into Defendants' marketing.

16. The case study approach is appropriate for this research for several reasons. Defendants' marketing must be examined in a real-world context to understand the practical aspects of it, and case study methods are ideal for this purpose.[5] In addition, the case study methodology is

[4] The interpretation of the data developed in a case study can also be described as inductively inferring meaning to the data.

[5] See e.g., related to the case study method, Gerring J. What Is a Case Study and What Is It Good For? American Political Science Review; May 2004; 98,2:341-354; Charles Schell, The Value of the Case Study as a Research Strategy, Manchester Business School, January 1992, available at: http://finance-mba.com/Case%20Method.pdf; Case Study Research Design and Methods, Second Edition, Robert K. Yin, Sage Publications, 2004; Yin, R. The Case Study Crisis: Some Answers. Administrative Science Quarterly, March 1981;26:58-65; David, D. Case Study Methodology: Fundamentals and Critical Analysis. Cognition, Brain, Behavior, 2007;11:299-317.

also appropriate for this analysis because in most forms of research control over subjects is required and that is not possible here. Further, an extensive body of literature exists related to pharmaceutical marketing which provides a theoretical basis for explaining the impact of opioid marketing on the medical community. These considerations suggest and validate the use of a case study research methodology. Finally, the case study method is widely accepted and utilized for research in teaching, business and marketing applications, and within the medical community.[6]

17. In this case, I was asked to assess the significance, if any, of Defendants' marketing related to prescription opioids. This was the overarching research question and problem to be addressed in this case. In this regard, I was also asked to address the following supplemental questions:

- What is pharmaceutical marketing?
- What are the basic standards or rules, if any, that the companies which market prescription opioids should follow?
- What were the Defendants' marketing strategies with respect to prescription opioids?
- How were marketing strategies implemented and marketing messages disseminated by Defendants with respect to prescription opioids?
- What were Defendants' messages?

[6] See e.g., Flyvbjerg B. Five Misunderstandings About Case-Study Research. Qualitative Inquiry, 2006;12(2):219-245; Kunselman J, and Johnson K. Using the Case Method to Facilitate Learning. College Teaching, 52(3):87-92; Trejo-Pech C and White S. The use of case studies in undergraduate Business Administration. Revista de Administração de Empresas July 2017;57(4):342-356; Bonoma T. Case Research in Marketing: Opportunities, Problems and a Process. Journal of Marketing Research, May 1985;26:199-208; Grigoryan, Y. Some aspects of teaching the history of medicine: the case study method. History of Medicine, 2017;4(3):237-242; Bridgman T, Cummings S, and McLaughlin C. Restating the Case: How Revisiting the Development of the Case Method Can Help Us Think Differently About the Future of the Business School. Academy of Management Learning & Education, 2016;15(4):724-741; David, D. Case Study Methodology: Fundamentals and Critical Analysis. Cognition, Brain, Behavior, 2007;11:299-317.

- What happened as a result of any opioid marketing?

18. Guided by marketing principles, the pharmaceutical marketing literature, and the research questions, I formulated propositions that were either supported or negated by the record (documents and testimony) creating data points. These data points were then linked to the study questions, interpreted in the context of both the case and the literature on pharmaceutical marketing. My commentary, findings, and conclusions are recorded in this Report.

19. In addition to the documents and testimony provided to me,[7] I searched for and identified additional documents in the Relativity database that I considered or relied on in my analysis.[8] A complete list of the materials relied on or considered is attached hereto as Schedule 3 to this Report. Specific documents that are used as examples to support my opinions are cited by Bates numbers. My opinions in this Report address Defendants' marketing activities and are stated to a reasonable degree of certainty in the field of pharmaceutical marketing.

COMPENSATION

20. I am being compensated at the rate of $350 per hour for my time related to this Report and a rate of $500 per hour for my time devoted to testimony. My curriculum vitae, which contains a list of my publications, is attached as Schedule 1. A list of cases in which I have testified in the previous four years is attached as Schedule 2.

[7] The documents provided to me were selected in part based on a set of "search" terms that was created by me and provided to Plaintiffs before my analysis began (Schedule 4: Perri's Document Search Terms).

[8] It is my understanding that I have been provided all deposition testimony, to date, in this matter. A listing of the depositions provided to date is included in Schedule 3: Facts or Data Considered.

OPINIONS

I hold the following opinions in this matter:

Opinion 1: Marketing is the process of creating value for customers through exchange. (In this Report, I will refer to customers of the pharmaceutical industry as "Customers."[9] When referencing general marketing principles, I will employ the term "customer.") Marketing is an integrated process of analysis, planning, implementation, and evaluation. Marketers analyze internal and external aspects of their businesses to identify opportunities in the marketplace. The marketers' goal is to create satisfaction and value and to increase sales.

Opinion 2: Defendants[10] are sophisticated marketers who are skilled in applying marketing strategy and tactics to successfully target and reach their desired Customers. This sophistication is seen in the pharmaceutical industry's strategic orientation, Customer-focused philosophy, extensive Customer data, well-integrated marketing activities, and extensive internal marketing communication.

Opinion 3: Pharmaceutical marketing targets Customers to increase the number of prescriptions sold for marketed products.

Opinion 4: Marketing principles establish standards, regardless of the type of product marketed. Pharmaceutical marketers should adhere to heightened standards of responsibility when marketing medicine, including:

[9] The customers of a pharmaceutical company's marketing activities include patients, prescribers, insurers, third-party payers, pharmacy benefit managers, and others who impact medication use and sales (e.g., pharmacies, pharmacists, wholesale distributors). Prescribers includes all who can write prescriptions for patients, including physicians, nurse practitioners, physician assistants, dentists, and any others with prescribing authority.

[10] This includes all Defendants in this case (see Schedule 5, Defendants in Case Track One), which all operate within the pharmaceutical supply chain system and all play a role in marketing the opioids at issue in this case.

a. Pharmaceutical marketers should support and promote the safe use of medicines, putting patient safety before profit.

b. Pharmaceutical marketing must always be truthful. A pharmaceutical marketer must never make a false or misleading statement to the medical community, other stakeholders, or the public.

c. Pharmaceutical marketers must always accurately disclose information about the risks of their product, in addition to the benefits being marketed.

d. Pharmaceutical marketing efforts should not be disguised as scientific or education.

e. Pharmaceutical marketing should be based on good-science to provide an unbiased, non-commercial basis for the use of medication.

f. Pharmaceutical marketers should be transparent about who or what they financially support.

Opinion 5: Defendants' marketing failed to adhere to industry standards in their marketing of opioids.[11]

[11] The list of drugs at issue in this case are listed in Schedule 6: ARCOS Opioid Drugs and Defendant Corporate Groupings – Contacts, Wholesale Dollars, and Retail Extended Units and MMEs, 1993-2018, and Schedule 7: ARCOS Opioid Drugs – Contacts, Wholesale Dollars, and Retail Extended Units and MMEs, 1993-2018.

Note: while there is a technical distinction between opiates and opioids, I will refer to the entire class of drugs that are at issue in this case as "opioids." Generally, the term opioid describes all compounds that work at opioid receptors. The term opiate refers to the naturally occurring alkaloids in opium, which is harvested from the flowering poppy plant: morphine, thebaine, papaverine and codeine. Opioid drugs may be derived from the natural opiates such as heroin, hydrocodone and oxycodone, and these are sometimes referred to as semi-synthetic opioids. Fully synthetic opioids are created entirely in the laboratory, such as fentanyl and methadone.

Opinion 6: Defendants executed their marketing strategy using similar marketing techniques and marketing messages. Marketing by the Defendants was consistent across Defendants in the message themes, and routes of communication with Customers:[12]

a) Dependence, tolerance, addiction, and withdrawal should not be a concern in prescribing opioids.

b) Opioids are effective for, and improve functioning in, patients taking them for long-term and chronic use.

c) Opioids should be first-line therapy for pain.

Opinion 7: Through execution of Defendants' marketing, the market for prescription opioids expanded.

BASIS AND REASONS FOR OPINIONS

I. MARKETING AND PHARMACEUTICAL MARKETING

A. Principles of Marketing

The Marketing Process

21. Marketing is the process of creating value for customers through exchange.[13] [14] Marketers strive to illustrate the value of their products by communicating how those products can fulfill existing needs and wants to create demand for their products. If they are successful in creating demand for their product, they receive an exchange of money through sales. Value is a subjective evaluation made by customers, assessing how well the perceived benefits outweigh any

[12] There were multiple marketing messages associated with each of these themes. These messages are identified and discussed in Section III of this Report.

[13] See e.g., Kotler, P and Armstrong, G. *Principles of Marketing*. 17th Ed. 2018, Pearson; Rollins, Brent L and Matthew Perri. *Pharmaceutical Marketing.* Jones & Bartlett Learning, 2014, p.4.

[14] In this discussion of the marketing process I refer to the customer as anyone for which a marketer seeks to create value.

perceived risks of the product and deciding that, in the end, the product was worth the price paid (perceived costs).[15] In exchange for value, customers provide sales revenue.

22. Marketing is an integrated process reflecting strategic and operational planning and implementation. (See Figure 1.) The starting point in marketing is to understand the company's mission and vision. Once formulated, marketers analyze internal and external aspects of their businesses to identify opportunities in the marketplace.[16] The information developed from the pre-market analyses is used to segment and target customers, set marketing goals, and to develop marketing strategy. Marketing strategies are then implemented, and the results obtained are evaluated to provide feedback to the marketing planning process. The goal of the marketer is to solve customers' problems, create satisfaction and value, thus selling more product.[17] [18] The documents and testimony reviewed in this case study examined each component of Defendants' marketing process, providing either support for or against propositions that ultimately describe Defendants' marketing behavior.

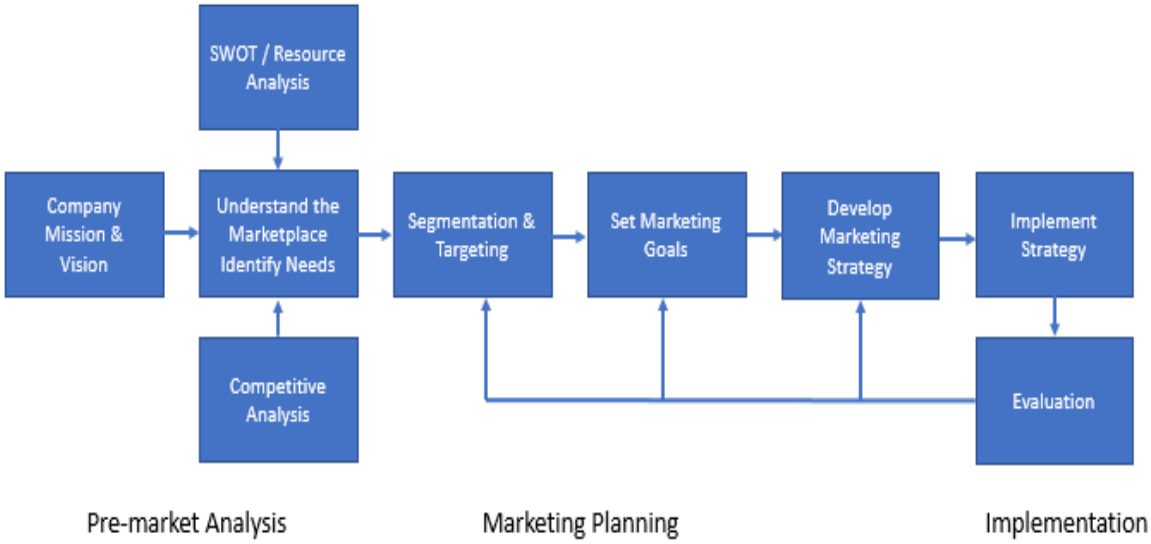
[15] Value may be represented as the subjective relationship between the perceived benefits and perceived costs of a product: Value = Perceived Benefit(s) / Perceived Cost(s). Higher value exists where the benefits are greater than the associated costs.

[16] This process is generally referred to as pre-market analysis. See e.g., Kotler P. Marketing Mix Decisions for New Products. Journal of Marketing Research 1964; 1(1):43-49.

[17] Marketers seek to satisfy a customer need and in doing so, solve customers' problems. When the product does a good job of solving customers' problems, it may represent a good value and provide customer satisfaction. I frequently use an analogy in my marketing teaching. With respect to electric drills, customers do not buy "drills," they buy holes. The hole is the solution to their problem which meets a need, if the price is reasonable it may represent a good value and ultimately satisfaction. Value is assessed subjectively and relates to the trade-off between how well the product worked and the price demanded. Defendants also recognized the need to solve customers' problems and the value proposition, see e.g., INSYS-MDL-008000539.

[18] See e.g., Kotler, P and Armstrong, G. *Principles of Marketing*. 17th Ed. 2018, Pearson; Kotler P and Keller K. Marketing Management. Boston: Pearson, 2016, 692 pages.

Figure 1: The Marketing Process



Creating Value with the 4Ps

23. When creating value for customers, marketers make decisions that revolve around the basic principles, or cornerstones, of marketing: the product or what will be sold (product); its price (price); how and where it will be sold (place); and how customers will be informed and persuaded about the product (promotion). These principles are referred to by marketers as the four "Ps" (4Ps) of marketing or the "marketing mix" variables.[19]

24. Each marketing decision is tethered to one or more of the 4Ps of the marketing mix. Further, successful marketers manipulate all the Ps of the marketing mix in order to maximize the effect of their marketing program.

[19] Some marketers like to consider additional Ps in the marketing mix, to include positioning, process (or packaging), and people. These product considerations are inherent to other marketing principles such as segmentation, targeting, and positions (discussed further infra) and are therefore included in the "mix" regardless of how they are classified. See e.g., Ahmad Kareh, Evolution of the Four Ps: Revisiting the Marketing Mix. Forbes. Jan 3, 2018. https://www.forbes.com/sites/forbesagencycouncil/2018/01/03/evolution-of-the-four-ps-revisiting-the-marketing-mix/#9c823aa11200 (last accessed November 29, 2018); Brian Tracy, The 7Ps of Marketing. Entrepreneur, May 17, 2004. https://www.entrepreneur.com/article/70824 (last accessed December 4, 2018).

Marketing Metrics

25. Marketers assess how well marketing is working using a variety of metrics such as sales, customer satisfaction, or less tangible metrics like brand loyalty or goodwill. Marketing metrics provide an additional input to the marketing process so that plans can be revised and adjusted to ensure the desired results are obtained.[20]

Segmentation, Targeting, and Positioning

26. The 4Ps and target marketing, which includes segmentation, targeting, and positioning, provide the foundation upon which marketers build their programs and can be described as:

- ***Positioning:*** Creating a perception in the minds of customers.[21] Positioning is critical to a product's success; the marketer's goal is for the product to be thought of first and favorably.[22] To achieve this, the marketer informs customers about product features and how these features translate into customer benefits to create the desired position in customers' minds.

- ***Segmentation:*** It may be difficult for one set of marketing decisions (revolving around the 4Ps) to create value for all customers. Therefore, marketers seek groups of customers with similar needs (and wants) and group these customers together into market segments.[23] For each market segment, decisions can be made that will appeal to these groups (segments) of customers with homogeneous needs.

- ***Targeting:*** Marketers have multiple segments of customers that can be considered for marketing efforts. A market segment that is selected to be the focus of marketing

[20] Seggie S, Cavusgil E, and Phelan S. Measurement of return on marketing investment: A conceptual framework and the future of marketing metrics. Industrial Marketing Management. 2007:36;834-841.

[21] See e.g., Kotler and Armstrong, Part 1, Chapter 2.

[22] Positioning statements are communicated in the marketing and tactical plans cited in this Report. These statements include goals such as "Become the first choice branded LAO in current and emerging customer segments." END00717275 p.21; Purdue positioned its OxyContin as "The one to start with, the one to stay with."

[23] See e.g., Sales Force Metrics, PPLPC029000132250 p.5.

activities is considered a "target" customer. The selection of target customers and efforts to reach these customers is referred to as "targeting."

27. The "science"[24] of marketing is complex and requires marketers to understand customers, what they need, and how they will react to marketing efforts.[25] While the basic principles of marketing lay a foundation, effective marketing also requires an understanding of psychology, consumer behavior, and the ability to adapt as products, customers, and the marketplace change.

28. Effective marketers understand and routinely employ the basic principles of marketing described above. Sophisticated marketers additionally have a clear strategic orientation, customer-oriented philosophy, ample information about their customers, a well-integrated company-wide marketing effort, and demonstrate excellent intra-organizational efficiency (e.g., communication, coordination) regarding the entire marketing effort.[26]

B. Pharmaceutical Marketing

Why Pharmaceutical Marketing has a Heightened Standard

29. Pharmaceutical marketers rely on the same basic marketing principles as the marketers of other consumer goods, but pharmaceutical marketing has important differences, including:

[24] Endo Pharmaceuticals had a department or division entitled, "Marketing Science," ENDO-CHI_LIT-00547242; Vitanza-Squires,K_ENDO, p.145; Defendants and others made reference to this kind of department, such as: ALLERGAN_MDL_00950093, Acquired_Actavis_01866272, ALLERGAN_MDL_04329034, (GfK) TEVA_MDL_A_02819649, (IMS) TEVA_MDL_A_08089140. Even pharmaceutical distributors recognize the science of marketing, as seen in CAH_MDL2804_00694748.

[25] Marketing research (sometimes referred to as consumer research or consumer behavior) is an important subset of marketing. Without good consumer level research, marketers cannot understand customers' needs or how their products can meet these needs. See e.g., Blackwell R, Miniard P and Engel R. Consumer Behavior, Ohio: Thomson Learning, 2001.

[26] See e.g., Kotler P. From sales obsession to marketing effectiveness. Harvard Business Review, 1977: (Nov-Dec);67-75; Kotler P. Marketing Management: Analysis, Planning and Control. Englewood Cliffs, NJ: Prentice Hall, 1988.

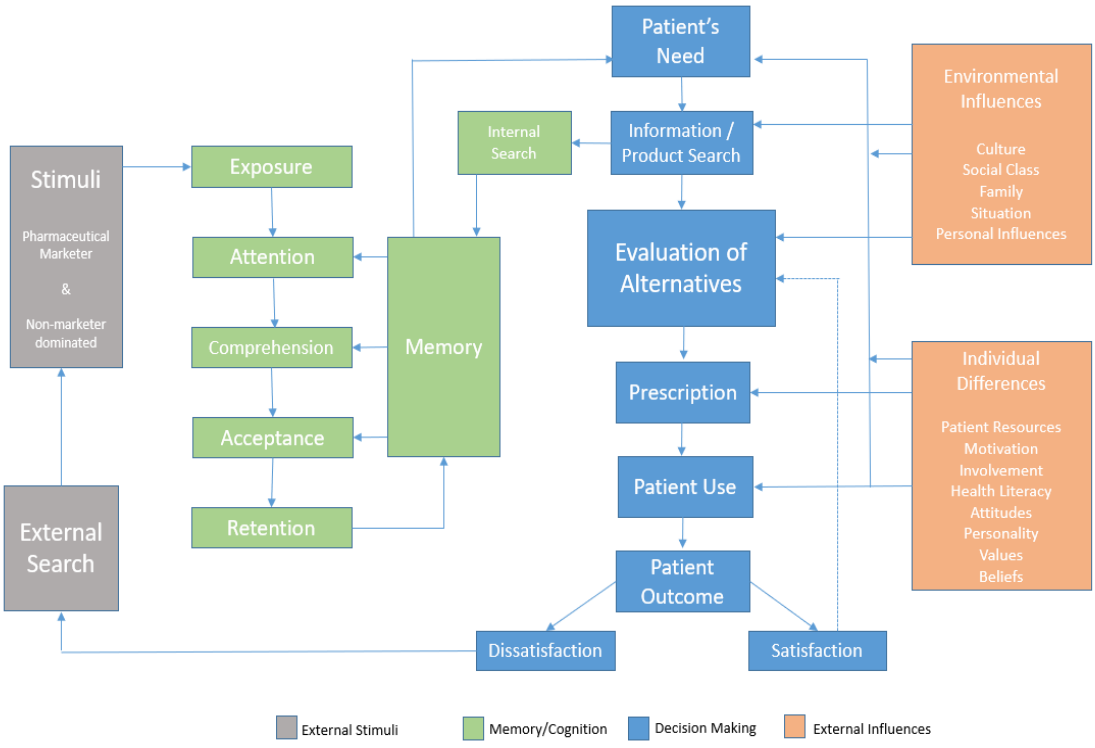
- Pharmaceutical marketing carries with it a heightened responsibility, because the "products" affect patient health and can be a matter of life and death.
- Prescription drugs carry with them risks that are as important as the benefits. This is especially true when the product being marketed is, by definition, dangerous to use, such as a Schedule II or Schedule III narcotic with serious side effects that can include addiction and death.[27] [28]
- The consumer (patient) who uses the product is not the person who selects the product; selection is made by a prescriber.
- Insurers, third party payers (TPPs), and pharmacy benefit managers (PBMs) influence the medication choices available to prescribers through formularies and preferred drug lists, which makes these stakeholders critically important to pharmaceutical marketers.
- Pharmaceutical marketers take advantage of the medical community's reliance on scientific evidence by not only providing science-based messages directly through their marketing, but also through funding and sponsoring clinical research, clinical practice guidelines, and continuing medical education.

[27] www.dea.gov/drug-scheduling (last accessed February 18, 2019).

[28] CAH_MDL2804_02882791, composite document beginning with: Internet Pharmacy Data, Meeting with Cardinal Health, Inc. DEA Headquarters, August 22, 2005. This document produced by Cardinal health supports the proposition that Schedule II – V drugs warrant special consideration with respect to marketing. The document which cites from a 1943 legal case, *Direct Sales Co. Inc. v United States,* includes at p.77 (p.4 of the case) states: *"But this is not to say that a seller of harmful restricted goods has license to sell in unlimited quantities, to stimulate such sales by all the high-pressure methods, legal if not always appropriate, in the sale of free commodities; and thereby bring about subversion of the other forms, which otherwise would protect him, and violation of the Act's other restrictions. Such a view would assume that the market for opiates may be developed as any other market. But that is not true. Mass advertising and bargain counter discounts are not appropriate to commodities so surrounded with restrictions. They do not create new legal demand and new classes of legitimate patrons, as they do for sugar, tobacco and other free commodities. Beyond narrow limits, the normal legal market for opiates is not capable of being extended by such methods. The primary effect is rather to create black markets for dope and to increase illegal demand and consumption."*

- Direct-to-consumer (DTC) prescription drug marketing seeks to influence patient demand for a medication by increasing patient awareness and creating the belief in patients' minds that they have a "right" to be treated with a specific drug.
- The decision to choose a medication is complex and influenced by marketers, the prescribing decision-maker, environmental, and individual influences. (See Figure 2: Physician Prescribing - Information Processing Model).

Figure 2: Physician Prescribing - Information Processing Model (Adapted)[29]



Concerns with Opioid Marketing

30. While pharmaceutical marketing itself is different than other product marketing, marketing for highly addictive schedule II narcotics has additional concerns not found with other medications

[29] Blackwell R, Miniard P and Engel R. Consumer Behavior, Ohio: Thomson Learning, 2001.

with less serious consequences. Renowned cardiologist and author, Dr. Isadore Rosenfeld (1927-2018), who came to be known as "America's Doctor,"[30] often said in public interviews that all medicines contain a little bit of "poison" meaning all medications confer some risk in addition to their benefits. This axiom applies to all medicines, but especially to the most dangerous classes of medications, including narcotic prescription opioids.

31. Because of the potentially dangerous nature of pharmaceuticals, pharmaceutical marketers are expected to put patient welfare first when making marketing decisions about prescription medicines. This is especially true for products like prescription opioids which should be treated differently in marketing compared to other consumer products, or even other prescription drugs, because of their serious side effects and the potential for abuse and diversion.[31] Given these concerns, Customers, including prescribers and formulary decision-makers (e.g., TPPs or PBMs), must have complete and accurate information to determine appropriate use.[32]

32. Additionally, because prescription opioids may result in tolerance, dependence, and/or addiction, the overall "demand" for opioids is distorted by pharmaceutical marketing aimed at increasing the use of these drugs. I refer to this as a distortion because, whether due to tolerance, dependence, or addiction, some patients who use opioids require and/or seek more opioids over time. These properties of opioids may also stimulate some users to report successful treatment to prescribers due to a desire or need to keep taking the drug. Therefore,

[30] Isadore Rosenfeld, Obituary. The New York Times, February 4, 2018. https://www.legacy.com/obituaries/nytimes/obituary.aspx?n=isadore-rosenfeld&pid=188070719 (last accessed December 13, 2018). Dr. Richard Sackler wrote to Dr. Rosenfeld in March of 2001 providing direct guidance on using OxyContin. Dr. Sackler stated the following: "the dose that works is the dose that is "right,"" oral oxycodone is "2 x as potent as morphine, 3 x as potent as hydrocodone….and ½ as potent as hydromorphone." He described conversion and titration in more detail. As noted later in this Report, Purdue had a bias toward benefits over harms in its communication with Customers. This email makes no mention of abuse risk for OxyContin (PDD9316504337).

[31] See e.g., Drug Scheduling https://www.dea.gov/drug-scheduling (last accessed February 28, 2019); See also, e.g., Wright, C_Purdue Deposition, pp.103-105 where he describes diversion as issues present with opioids since at least 1993.

[32] See e.g., Mintzes B, Lexchin J, Sutherland J, Beaulieu M, Wilkes M, Durrieu G, and Reynolds E. Pharmaceutical Sales Representatives and Patient Safety: A Comparative Prospective Study of Information Quality in Canada, France and the United States. J Gen Intern Med 28(10):1368-75.

the use of the opioids can result in an increase in demand for opioids. This increase in demand effectively expands the overall market for these drugs – in addition to creating demand for the advertised product.[33]

33. Pharmaceutical companies employ marketing because it helps to achieve the sales objectives created for their businesses and products. However, marketing in and of itself is a tool, and is therefore without conscience, ethical, or moral judgment. Thus, marketing strategies and tactics should be used carefully by individuals who must consider the appropriateness of their actions.

Standards that Apply to Pharmaceutical Marketing

34. In all pharmaceutical marketing activities, pharmaceutical marketers must comply with standards set by the government requiring them to work within their FDA approved labeling when communicating marketing messages to Customers. In addition to existing laws or guidelines, multiple organizations and associations from the U.S. and around the world have published guidelines, opinions, and ethical principles that should be voluntarily followed by pharmaceutical companies in order to overcome the challenge inherent to this industry: how to put patients first while still making a profit for shareholders.[34]

35. Pharmaceutical companies seeking appropriate medication use should all agree that the goal is for medications to be used correctly and to provide maximum benefit to patients. Therefore,

[33] Market expansion was a strategic goal of Defendants, see e.g., PPLPC016000255303, BDC meeting-Project Tango.

[34] See e.g., Editorial. Ethical challenges in the pharmaceutical industry. Prof. Jose Luis Valverde, Editor in Chief, Pharmaceuticals, Policy and Law. 2012: 14; 123-127. "The ultimate ethical goal in the pharmaceutical industry is to discover and develop safe and efficacious drugs that allow patients to live longer, healthier and more productive lives, while making a profit to reward shareholders and to invest in research for the next generation of medicines." Haque, O, De Freitas J, Bursztajn H, Cosgrove l, Gopal A, Paul R, Shuv-Ami I, and Wolfman S. The Ethics of Pharmaceutical Industry Influence in Medicine. May 2013, UNESCO Chair in Bioethics Office, Publications Division, Ministry of Education, Israel (ISBN 9897-965-444-035-6);

companies seeking appropriate medication use should follow basic standards, in addition to laws and guidelines in their marketing conduct, summarized in the following statements:[35] [36]

- Pharmaceutical marketers should support and promote the rational use of medicines, putting patient safety before profit.

[35] See e.g., Laczniak G and Murphy P. Normative Perspectives for Ethical and Socially Responsible Marketing. Journal of Macromarketing 26(2):154-177; Haque, O, De Freitas J, Bursztajn H, Cosgrove l, Gopal A, Paul R, Shuv-Ami I, and Wolfman S. The Ethics of Pharmaceutical Industry Influence in Medicine. May 2013, UNESCO Chair in Bioethics Office, Publications Division, Ministry of Education, Israel (ISBN 9897-965-444-035-6); Editorial. Ethical challenges in the pharmaceutical industry. Prof. Jose Luis Valverde, Editor in Chief, Pharmaceuticals, Policy and Law. 2012: 14; 123-127; Komesaroff P and Kerridge I. Ethical issues concerning the relationships between medical practitioners and the pharmaceutical industry. Medical Journal of Australia, 2002; 176:118-121; Association of the British Pharmaceutical Industry (ABPI). Code of practice for the pharmaceutical industry 2016. London: Prescriptions Medicines Code of Practice Authority, 2016; Code on Interactions with Healthcare Professionals. Pharmaceutical Research and Manufacturing Association (PHRMA). http://phrmadocs.phrma.org/sites/default/files/pdf/phrma_marketing_code_2008-1.pdf; CBS MoneyWatch, November 30, 2007, Understanding Marketing Ethics. https://www.cbsnews.com/news/understanding-marketing-ethics/ (last accessed November 7, 2018); Ethical criteria for medicinal drug promotion. Resolution WHA41.17, World Health Organization, Geneva, 1988, http://apps.who.int/medicinedocs/documents/whozip08e/whozip08e.pdf (last accessed November 7, 2018); Pan American Network on Drug Regulatory Harmonization, Working Group on Medicines Promotion. Ethical criteria for the promotion, advertisement, and publicity of medicines. Pan American Health Organization/World Health Organization. http://apps.who.int/medicinedocs/documents/s22161en/s22161en.pdf (last accessed December 13, 2018); International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) Code of Practice 2012, Guiding Principles on Ethical Conduct and Promotion, http://apps.who.int/medicinedocs/documents/s22329en/s22329en.pdf (last accessed December 13, 2018);

[36] When asked, Defendants also provided support for these propositions. See e.g., Boyer, Andrew_Teva Deposition, p.305; Condodina, Cynthia_Teva Deposition, pp.482-483; Ritchie.Bruce.Janssen.1.25.2019 Deposition p.49; Shusterman, Neil_Endo2019.1.18 (Day 2) Deposition, pp.626-627; Stacy Chick 121318 Deposition, pp.126-130; Storey_Purdue Deposition, pp.74-76; Terifay, Terrence_MNK Deposition, pp.478-480; Udicious,Thomas.Insys.1.24.2019 Deposition, p.72; Barrett_Allergen (sic) Deposition, p.32; Beckhardt.Stacey.Teva.2.1.2019 Deposition, p.59; Craven.Colleen.Endo.2.6.2019 Deposition, pp.145-146, 446; McGregor-Beck, Roxanne_Janssen Deposition, pp.46-47, 294, 339-340, 347; Phillips.Lynn.MNK.2.12.2019 Deposition, p.65; Wessler, Michael_MNK Deposition pp.67-70; Bingol, Demir_Endo Deposition, p.339; Barto.Robert.Endo.1.30.2019 Deposition, pp.62-64; Cramer, Phil 11.20.18 Deposition, pp.193-194; Gasdia_Purdue Deposition, pp.213-214; Vorderstrasse_MNK Deposition, p144; Cramer, Phil_11-20-18 Deposition, p.189; O'Neill, Hugh_MNK (EVP, Chief Commercial Officer) Deposition, pp.135-139.

- Pharmaceutical marketing must always be truthful. A pharmaceutical marketer must never make a false or misleading statement to the medical community, other stakeholders, or the public.
- Pharmaceutical marketers must always accurately disclose information about the risks of their drug, in addition to the benefits being marketed.
- Pharmaceutical marketing efforts should not be disguised as scientific or educational.
- Pharmaceutical marketing should be based on good science to provide an unbiased, non-commercial basis for the use of medication.
- Pharmaceutical marketers should be transparent about who or what they financially support.[37]

Messages, strategies, and techniques used by pharmaceutical marketers must all comply with these basic propositions that describe the higher standard for pharmaceutical marketing conduct.

Defendants are Effective Pharmaceutical Marketers

36. I have reviewed an extensive record of documents and testimony related to each aspect of Defendants' marketing, reflecting an array of marketing efforts. It is my opinion that Defendants were sophisticated in their application of marketing principles and strategies to generate demand for their drugs. The documents I reviewed demonstrated a high level of customer-centric, strategic orientation, strategic planning, integration of marketing within their organizations, and extensive intra-organizational communication regarding marketing activities. In my opinion, Defendants were sophisticated in their application of proven marketing techniques to achieve their marketing goals.

[37] For example, who is paid to endorse their product, what research the company has funded, who has been paid to advocate for the product, etc.

Setting Pharmaceutical Marketing Strategies

37. A marketing plan is a comprehensive description of the full scope of marketing activities, or the road map, used to achieve sales and profits. Marketing plans identify strategies, set goals, and plan for the implementation and evaluation of marketing activities and are developed at multiple levels within the organization. Marketers base their plans on careful assessment of a company's strengths and weaknesses as well as the opportunities and threats (SWOT analysis) that exist within the business environment. This information is integrated with resource analysis and the assessment of market potential, to identify areas of business opportunity and to formulate corporate marketing objectives.

38. Once corporate direction has been established, marketers develop organization-wide marketing planning efforts. These efforts range from the highest-level plans where corporate level strategy is set, to regional, territory, and even individual level plans. The mid- and lower-level plans are more operational and focus on implementation. All marketing planning activities, when considered together, create a purposeful and strategic action plan that a company will use to achieve its desired results.

Pharmaceutical Marketing's Target Customers

39. Pharmaceutical marketers seek to drive the sales of prescription drugs by educating and persuading target Customers about the value of the marketer's drug. Target Customers include prescribers, payers (insurers, third party payers, pharmacy benefit managers), sites of care (e.g., institutions, long term care, retail, or surgery centers), and influencers (e.g. professional and patient advocacy groups, employers, thought leaders, or policy makers).[38] Physicians and other

[38] There are numerous marketing plans and related business documents and communications in this matter which outline messages, targets, and tactics for reaching selected target markets, See e.g., Advocacy, Policy, Quality Activities. Engage advocacy partners to help define patient treatment success & access pain management options. Nucynta (Tapentadol), JAN00038605; 2008-20012 Opana Brand Tactical Plan, August 15, 2007, END-CHI-LIT-00076051; Coviden: Positive Results for Life 2011-2015 Strategic Plan, May 28, 2010, MNK-T1_0000468961; Managed Care Cap-Sells August 23, 2005, PPLPC008000042911; 2012 Budget Presentations Commercial Overview, Russ Gasdia Vice President Sales

prescribers are primary targets of pharmaceutical marketing efforts because patients cannot write prescriptions, and, generally, do not possess the technical knowledge to diagnose a medical condition and choose between alternative prescription medications.[39] However, the pharmaceutical industry does employ DTC promotions which encourage patients to ask their physician about drugs they have seen advertised.[40]

40. Yet, for most drugs, pharmaceutical marketers target those who make decisions about which medications will be used by patients, namely, the prescribers, insurers, TTPs, PBMs, and formulary decision-makers.[41] The record in this case certainly supports the proposition that

& Marketing, PPLPC008000067059; 2003 Actiq Marketing Plan, TEVA_CHI_00042882; MoxDuo Launch Preparation, Actavis Inc., ACTAVIS0318876; Lombardo June 8, 2006 email with subject: FW: OxyContin Reimbursement Alert – Coventry Health Plan, PDD8800013331; Mallinckrodt-Wickline-007. 30300-Ohio Business Plan "Go Where You Can Grow"; ENDO-OPIOID_MDL-02344002 (Hospitals, LTC, ambulatory care, rehab, etc.) p.E0256.11; EN3288 Launch Plan, August 2009, ENDO-CHI_LIT-00018061.

See also, e.g., PHRMA Pharmaceutical Marketing in Perspective, brochure, http://phrma-docs.phrma.org/sites/default/files/pdf/phrma_marketing_brochure_influences_on_prescribing_final.pdf (last accessed December 1, 2018).

[39] Other stakeholders who can impact prescribing may include, for example: drug utilization review board and pharmacy and therapeutics committee members, insurers and third-party payers, formulary managers, or pharmacy benefit managers.

[40] The goal of DTC is to generate awareness on the part of patients (and prescribers, other stakeholders, and influencers, because they are also consumers and exposed to DTC efforts) and create dialog between patients and prescribers with the expectation of generating a prescription. Pharmaceutical marketing also targets consumers and caregivers indirectly through its support of patient and disease advocacy groups. DTC efforts can take the form of disease education, self-help messages, unbranded advertising, and public service or public relations efforts. Related to public relations, see e.g., JAN-MS-01239357, Kuntz depo. Ex. 11, Ketchum Vendor Accrual Dec 2007 email chain; JAN-MS-01239328, Kuntz depo. Ex. 12, Tapentadol 2007 PR Accomplishments.

[41] Insurance companies and pharmacy benefit managers (PBMs) are involved in creating mechanisms in the pharmaceutical supply chain to provide insurance coverage and payment to pharmacies for insured patients. If drugs are not listed on formularies, or have barriers to use, they will be used less. This gives insurers, third party payers, pharmacy benefit managers, and formulary decision-maker's significant market power. This is discussed later in this Report. See also, e.g., Gasdia_Purdue Deposition pp.86-87, 98-100; Jollif_MNK Deposition p.200; Moskovitz_Janssen_Vol.1 & 2 30(b)(6) Deposition, pp. 271-275, 551; Spokane_TEVA Deposition p.240 and Exhibit 38; Storey_Purdue Deposition p.173 and Exhibit 15 (Product Information for Formulary Review Committee).

Defendants planned and worked diligently with multiple target audiences, including TPPs and PBMs to ensure and maintain formulary coverage for the opioids they marketed.[42] [43]

41. Every target Customer requires accurate information to critically evaluate medication alternatives. Much of the information available to stakeholders is either provided by, or influenced by, pharmaceutical marketers who seek to control the information in the marketplace that will create the desired position for their drug(s) in Customers minds.[44] [45] However, if the information provided by pharmaceutical marketers is flawed (e.g., incomplete, biased, based on weak science), false, or misleading, patients are put at risk because drugs may not be used appropriately. While flawed information can still impact the prescribing process and generate sales, it violates the basic standards in pharmaceutical marketing set forth above.

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[42] See e.g., 035_ALLERGAN_MDL_01283526, Kadian Co-Pay Assistance Program; Kadian Co-Pay Card, 148_ACTAVIS0205613; 2015 Opana ER Annual Plan, ENDO-CHI-LIT-00549855; ENDO Pharmaceuticals 2008-2012 Opana Brand Tactical Plan, EPI000560276; Nucynta ER $25 Savings Card, JAN-MS-00228916; Nucynta Savings Card ROI Evaluation, June 2010, JAN-MS-00259847; $50 Off, Duragesic, JAN-MS-00291469; Duragesic Coupon ROI Analysis, March 2002, JAN-MS-00311391; Subsys Strategy, especially p.28-29, INSYS-MDL-003271421; Offsite Strategic Planning Session, May 23, 2013, INSYS-MDL-003360259, pp.72-83; Nucynta IR SCG and SEPain Region Payer Planning, JAN-0019-0041290; 2012 Brand Investment Summary, JAN00019879; TEVA_CHI_00008900 p.25-28; OxyContin Launch Plan Proposal, PURCHI-003285039, p.10; EXALGO/PENNSAID Formulary Updates, MNK-T1_0000093660; Opana ER with INTAC 2013 Quarterly Business Review, ENDO00125324; Launch Readiness Review Market Access, July 30, 2010, JAN-MS-00815827; Achieving Pull Through Excellence: Driving Demand by Leveraging Access, 2012, JAN-MS-00858249; Tapentadol Pricing and Managed markets Strategy Recommendations, CRA International Report to J&J, JAN-MS-01130587; Xartemis XR Launch KPIs, MNK-T1_0000135090.

[43] Formulary decision-makers do not select a drug for the patient, but they decide which drugs will be available through its formulary. Drugs that are not covered, or which have barriers to use (e.g., prior authorization) will be used less. This gives formulary decision-makers the ability to move market share, and drive or limit demand in a market.

[44] See also, e.g., Barrett Allergan Deposition p.257; Deen_Eshleman_Janssen Deposition p.139.

[45] Pharmaceutical marketers seek to carefully control the messages that are created and disseminated about their products. This is evidenced in the Defendants' extensive and detailed marketing plans cited in this Report. However, as noted in the adapted prescribing information processing model presented above, non-marketer-controlled information, such as a patient advocacy group or a media article, is also present in the market-place and can also impact information processing by physicians. Marketers seek to ensure that the information emanating from sources such as these are consistent with its own carefully developed and internally approved messages. The marketer's desire to exert control over this non-marketer-dominated information explains, in part, why companies support patient or disease advocacy groups.

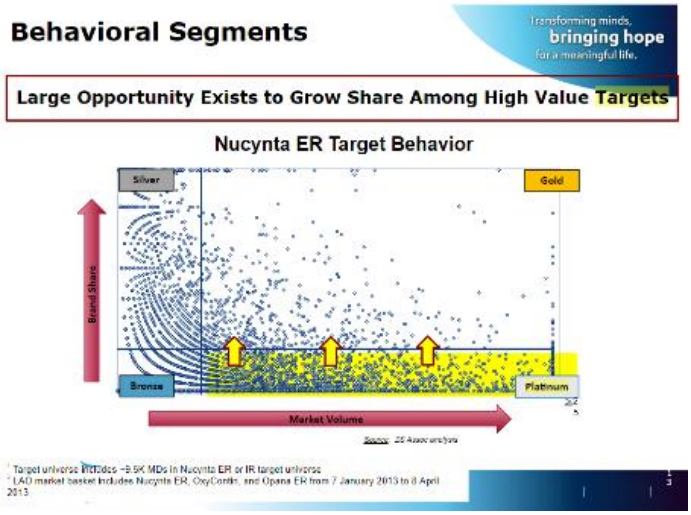
Prescribers

42. Marketers frequently target prescribers who are most likely to prescribe their drug. Marketers identify prescribers using commercially available data, which groups prescribers, for example, into deciles (1-10) reflecting lower versus higher levels of prescribing. Marketers use this information to select prescribers, or groups of prescribers, as target Customers. Targeting high decile (more frequent prescribing) prescribers is consistent with marketing principles because it effectively targets Customers with potential to generate sales. Defendants used "deciles" to identify the best physicians for their PSRs to use in sales-call planning.[46] [47] For example, targeting high prescribers was seen at Janssen where the conversion of "Platinum" Customers to

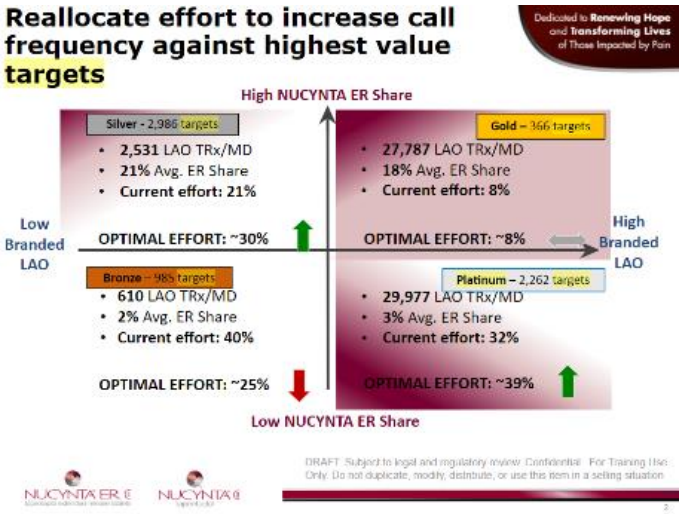
[46] The Defendants use of decile marketing was extensive as seen in numerous marketing planning and other documents. A few examples are provided here, e.g., Mallinckrodt-Wickline-015, p.E0501.29, E0501.61; "Putting it All Together" 2011 KADIAN® National Sales Meeting, ACTAVIS0543363 p12.; Altier email, 2/25/2013, RE: Kadian Targeting Analysis; Tolkacz email, 2/25/13 RE: Kadian Targeting Analysis, ACTAVIS0195728; Hutcheson email, 6/5/2012, AcutePain (sic) Specialty Decile 201112.xls, ACTAVIS0284119; Insys Offsite Strategic Planning Session, May 23, 2013, pp.17-21, INSYS-MDL-000103520; NUCYNTA® Launch Meeting (ERS), p.6, JAN00060148; XXR_OnDemandRepInvitation_081513, 8/15/14, MNK-T1_0000092452; (Purdue) Memo, to Doug Wheeler, 11/7/2001, p.2, E01-00011773; Grayson Memo, 5/2/2002, E01_00014068; Opana® ER Q4 2011 Quarterly Business Review, p.17, ENDO00002135; Fish where the fish are, see Wickline_MNK, pp.263-264; Bingol, Demir_Endo, p.265; Area Business Review, p.5,TEVA_FE00006281; PPLPC041000031311, September 13, 2013 slide deck "OxyContin growth opportunities - Phase I Final Report: Diagnostic"; Bingol, Demir_Endo Deposition, p.157; Boothe, Douglas_Allergan Deposition, p.166; Cramer,Phil 11-20-18 Deposition, p.20; Horowitz, E_Purdue Deposition, pp.137-138; Jackson, R_Endo Deposition, pp.215-220; Kaisen, Valerie_Teva Deposition, p.81; Lortie.Brian.Endo.1.22.2109 Deposition, pp.152-153; Ritchie.Bruce.Janssen.1.25.2019 Deposition, pp.91-92; Romaine, Larry_Endo Deposition, pp.239-241; Vorderstrasse_MNK Deposition p.201; Wickline_MNK Deposition, pp.261-266; At Purdue, PSRs were trained on how to write call notes that would not reflect negatively on the company. In one such training the use of the term "whale" to describe high prescribers was discouraged. Mr. Cramer also noted use of the term "Super Core" in reference to high decile prescribers. Cramer, Phil_11-20-18 Deposition, pp.22-23, 26-32, 40. Other Defendants referred to high prescribers as "platinum" targets (Burns_Janssen, pp. 208-225, Janssen, see also e.g., JAN-MS-00659575, Platinum Potentials Analytics p.15), "high decile" (all), "Fab Five" (Endo), Fab Five was reflective of a PSRs top five prescribers (Romaine, Larry_Endo p.271). See also, e.g., JAN-MS-00669512, Nucynta ER Segmentation Final Results; Jan-MS-00756523, Nucynta ER Target Optimization

[47] Fugh-Berman A, Ahari S. Following the Script: how drug reps make friends and influence doctors. PLoS Medicine 2007; 4(4):621-625.

"Gold" was analyzed[48] and allocation of sales force efforts on "highest" value targets was considered:[49]



Platinum Potential Analytics, JAN-MS-00659575



Nucynta Target Optimization, JAN-MS-00756523

[48] JAN-MS-00659575, Platinum Potentials Analytics, p.15.
[49] JAN-MS-00756523, Nucynta Target Optimization, p.2.

43. In addition to the use of deciles, Defendants also marketed to physicians in areas where opioid prescribing was already high, and where abuse was greater.[50] Targeting these high prescribers was key to Defendants ability to expand[51] the opioid market. However, Mr. Barto, who worked for a time in Regulatory Affairs at Endo, noted with respect to the use of deciles in targeting prescribers, *"the goal was not to grow the market but to take market share."*[52] From a marketing perspective, market expansion and capturing share (market penetration) are not mutually exclusive goals.

44. Additional factors in targeting prescribers may include prescriber specialty, accessibility, or prescribing patterns such as previous use of a company's drug(s) or individual characteristics.[53] To stay current on drug knowledge, prescribers need information. Marketers fill this need and Customers rely on the pharmaceutical industry to provide them with technical and science-based information that it is generally considered reliable.[54] Educational marketing efforts tap into the desire to make good decisions for patients that are based on reliable, valid, and unbiased information.

45. Indeed, pharmaceutical marketers take advantage of prescribers' scientific orientation[55] and need for information by sponsoring and distributing research results through peer-reviewed

[50] JAN-MS-00660589 and JAN-MS-00660588, Email and Nucynta Extended Team Meeting. Lin,D_Janssen Deposition pp.275-280; In conjunction with this, see the RiskMap document JAN-MS-01057540 where Janssen notes, *"Despite the regulatory controls that are in place to prevent the misuse, abuse, and diversion of Schedule II drugs, data show that as the number of prescriptions for opioid drugs increases, so does the frequency of misuse, abuse, overdose, and drug-related fatalities."*

[51] A market expansion strategy is one that offers a product (or service) to existing customers in new ways, or to new customers with the goal of increased sales. Regarding opioid medications, this could mean selling more opioids to existing patients or finding new patients to treat with opioids.

[52] Barto.Robert.Endo.1.30.2019 Deposition, pp.296-298.

[53] An individual characteristic might include a thought leader, or key opinion leader. Other physicians rely on these kinds of peers as a source of influence on their own prescribing. See e.g., Lubloy A. Factors affecting the uptake of new medicines a systematic literature review. Health Services Research 2014; 14:469-94.

[54] Fugh-Berman A and Ahari S. Following the Script: How Drug Reps Make Friends and Influence Doctors. PLoS Medicine 2007; 4(4):621-625.

[55] See Lubloy, 2014, cited above.

publications.[56] Peer-reviewed publications are generally perceived as unbiased, good-science,[57] which prescribers' value because it gives them confidence in the information they are receiving. This confidence is diminished when prescribers learn that literature is not based on good-science or contains commercial bias. Bad science that impacts prescribing puts prescribers themselves at risk. As discussed in Section III below (Defendants' Marketing of Opioids), Defendants relied on materials that did not always meet the standards for good-science.

Third Party Payers

46. Third Party Payers (TPPs) cover, or pay for, the cost of drugs that are listed in their formulary or preferred drug list (PDL) for beneficiaries.[58] Formularies and PDLs are usually developed and maintained by pharmacy benefit managers (PBMs) who may work independently or in conjunction with pharmacy and therapeutics committees or drug utilization review committees.[59] Formulary development involves deciding which drugs will be covered and which will not. Generally, if a drug is not covered, its utilization will be low or non-existent.

47. Formularies and PDLs are used in conjunction with tools like prior authorization, step therapy, various hard and soft utilization edits, and preferred formulary status to purposefully drive utilization to desired levels within a prescription benefit plan.[60] These additional tools are under the control of the TPP or PBM, giving these decision-makers ways to direct demand toward or away from a manufacturer's drug. Through the formulary development process, TPPs and PBMs

[56] See e.g., Kadian 2005 Publication Plan, ACTAVIS0006930.

[57] Good-science is a term of art that refers to research that adheres to principles that protect it from threats to reliability, internal and external validity.

[58] A formulary is a listing of the drugs approved for plan member reimbursement under the TPPs plan. Open formularies include all drugs. Closed formularies include only the drugs approved by the TPP. A preferred drug list includes all drugs but provides preferential treatment to drugs selected by the TPP.

[59] Influential physicians, thought leaders, and KOLs may also be members of pharmacy and therapeutics or other formulary development committees.

[60] For example, a drug may be covered, but the PBM can restrict utilization by placing the drug on "prior authorization" (PA) requiring prescribers or pharmacies to obtain permission to use the drug. PA is seen by industry as a potent barrier to sales and, therefore, industry representatives will work to avoid PA restrictions being placed on their drugs.

have a significant ability to drive market share by supporting the use of or creating barriers to utilization of a manufacturer's drug(s).

48. Integral to the formulary development process is the role of the pharmaceutical manufacturer in providing accurate clinical or economic evidence to TPPs and PBMs. This evidence may include drug labeling and other relevant clinical or economic research that manufacturers believe will support the use of their drugs.[61] Formulary developers may also seek other clinical information[62] to make decisions about drug coverage.

49. However, pharmaceutical marketers also rely on relationship[63] building and other indirect ways to influence a drugs inclusion on a formulary. For example, a manufacturer can indirectly exert marketing pressure on formulary decisions by using key opinion leaders as advocates for a drug and by supporting advocacy groups who want to ensure access to a specific drug.[64] This can impact formulary decision-makers because these stakeholders also have customers (i.e., employers, state Medicaid, insurers) and must make decisions consistent with their customers' desires. Other commercial influences, such as public relations, lobbying efforts, or company-sponsored research can also indirectly influence formulary decisions. Indeed, research has

[61] See e.g., MoxDuo Launch Preparation, April 13, 2012, ACTVAIS0304733; MoxDuo Launch Preparation, March 16, 2012, ACTAVIS0313491.

[62] Other clinical information might include, for example, relevant clinical experience possessed by members of the pharmacy and therapeutics committee, published clinical research, past utilization in the plan.

[63] Relationship marketing seeks to foster relationships with current or future customers by creating two-way dialog to meet the customer's needs, build customer loyalty and create an advocate (e.g., KOL or Thought Leader) for a brand. Relationship marketing helps ensure a positive experience with the brand and seeks to affect customer behavior.

[64] See e.g., documents like the 2012 Actavis MoxDuo Staffing Plan/SOW (ACTAVIS0316645) which describes a proposal to partner with the American Pain Society (or other relevant third-party group) to conduct research on the "Cutting Edge of Pain." This document describes numerous outreach activities that will be engaged including KOLs, news releases, advocacy "media" channels/e-newsletters/Twitter feeds, publication of "controlled" guest blogs, editorials, etc.; EN3288 Launch Plan August 25, 2009, ENDO-CHI_LIT-00018061 (KOLs). See also, Schedule 18: Amounts Paid to KOLs; Schedule 17: Amounts paid to Pain Advocacy Organizations & Professional Societies, Schedule 14: Manufacturing Defendants' Use of Advocacy.

shown that adoption of new drugs is impacted by these kinds of commercial influences which can impact formulary decisions.[65]

50. Pharmaceutical marketers rely on the fact that TPPs and PBMs need drug information to develop their formularies. Prescribers then rely on formularies, created in part with the pharmaceutical manufacturer's information, and its associated commercial influence when selecting a drug for a patient. Pharmaceutical companies who target TPPs and PBMs, therefore, have a strong influence on prescribing and a significant ability to drive a drug's market share.

51. When TPPs or PBMs do not give drugs' preferential status on a formulary or PDL, patients will have to pay more to access these drugs through higher copays or even bearing the full cost of the drug out-of-pocket. This creates a barrier to the use of medications which pharmaceutical marketers recognize.[66] Therefore, a common goal of the pharmaceutical marketer is to obtain

[65] Peay M and Peay E. The Role of Commercial Sources in the Adoption of a New Drug. Soc Sci Med 1988;26(12):1183-89; Sah S and Fugh-Berman A. Physicians under the Influence: Social Psychology and Industry Marketing Strategies. Journal of Law, Medicine and Ethics 2013;41(3):665-672.

[66] See e.g., June 8, 2000 Lombardo email with subject: FW: OxyContin Reimbursement Alert – Coventry Health Plan, PDD8800013331; Managed Care Cap-Sells, PPLPC0008000042911; Silva Memo to Houston District, Plantrak Analysis, PPLPC01000020169; August 15, 1997 Thatcher email with subject Maryland HealthChoice (Medicaid): FreeState health Plan, PPLPC012000002897; Exalgo/Pennsaid Formulary Updates, MNK-T1_0000093660; January 12, 2012, Wickline email with subject FW: Your mission: Operation Workers Compensation – District Strategy Meeting Follow-up, MNK-T1_0001476131; Opana ER Managed Care Pull-through Workshop, ENDO00019668; Opana ER Market Research (PSI Inc.), December 11, 2006, ENDO-CHI_LIT00547417; SCG and SEPain Region Payer Meeting, JAN-0019-004-1290, p.7.

See also, e.g., Puig-Junoy J and Moreno-Torres I. Impact of Pharmaceutical Prior Authorisation Policies: A Systematic Review of the Literature. Pharmacoeconomics, 2007; 25(8):637-648; Roughead E, Zhang F, Ross-Degnan D, and Soumerai S. Differential Effect of Early or Late Implementation of Prior Authorization Policies on the Use of Cox II Inhibitors; Clark R, Baxter J, Barton B, Aweh G, O'Connell E, and Fisher W. The Impact of Prior Authorization on Buprenorphine Dose, Relapse Rates, and Cost for Massachusetts Medicaid Beneficiaries with Opioid Dependence. Health Services Research, 2014; 49(6):1964-1979; Yu C, Soumerai S, Ross-Dengan D, Zhang F, and Adams A. Unintended Impacts of a Medicaid Prior Authorization Policy on Access to Medications for Bipolar Illness. Medical Care, 2010; 48(10):4-9; Kotzan JA, Perri M III, Martin BC. Assessment of Medicaid prior-approval policies on prescription expenditures: market share analysis of Medicaid and cash prescriptions. J Managed Care Pharm 1996; 2(6): 651-6.

preferential formulary position, without restrictions that would limit utilization.[67] When barriers exist, pharmaceutical marketers have responded with "coupons" and other strategies to reduce out-of-pocket costs to patients, thereby reducing or removing any barrier to utilization.[68]

Others

52. In addition to prescribers and third-party payers, other important targets of pharmaceutical marketers include, for example, patients and caregivers, policy makers, academic and clinical researchers, sites of care (e.g., institutions, long term care, retail, or surgery centers), and influencers (e.g. professional and patient advocacy groups, or employers). Defendants' marketing plans enumerate marketing efforts designed to reach each of these target markets.[69]

Common Marketing Techniques Used to Influence Prescribing

53. Pharmaceutical marketing encompasses a wide range of methods that are effective in generating demand for prescription drugs.[70] With a focus on prescribers who appreciate science, pharmaceutical marketing works best when it appears to be based on good-science. Good-

[67] See, e.g., November 2010, Strategic Customer Group, JAN-MS-00466015_Confidential, p.19; Nucynta Contracting Update, JAN-MS-00020777.

[68] See e.g., Kadian New Strengths Launch, ACTAVIS0263836 p.5; Nucynta $25 Savings Card, JAN-MS-00228916; $0 co-pay on first Rx., Pay no more than $25 Savings Card, JAN-MS-00229864; April 2010 REP DOC Market Research Cost Specific Findings, JAN-MS-00259847_2010; $50 off Duragesic, JAN-MS-00291469; Duragesic Coupon ROI Analysis, MarketRx, July 2002, JAN-MS-00311391; Opana ER Brand Plan 2009, p.15, ENDO-CHI LIT-00023297; PPLPC008000005359, p.45.

[69] While there are many marketing plans cited directly in this Report, Schedule 8: Manufacturing Defendant Marketing Plans, also provides a listing of Defendants' marketing plans.

[70] Pharmaceutical marketers may utilize outside vendors to provide marketing support services aimed at helping brands deliver their messages. This includes companies like Ascend, Green Room Communications, Mosaic, or Decile Ten which provide a variety of marketing support services, often with a focus on speaker training, such as KOLs. Services could include developing presentations, slide decks, honoraria, speaker training programs, sales aids, managing KOL databases, speaker's bureau activities. etc. See e.g, Deem_Eshleman_Janssen Deposition, p.85; Lin, D_Janssen Deposition, pp.196-199, 219-221; 319-321. These vendors can also assist with public relations efforts, e.g., Green Room Communications, 2104 memo to Rhonda Sciarra and Kevin Webb at Mallinckrodt on the "Cake Alliance for Balanced Pain Management Opportunity", MNK-T1_0000876637; Webb email with subject: Description of Jennifer Aniston Movie: Cake, MNK-T1_0000876825; MNK-T1_0000877241, Mallinckrodt "CAKE PR Recommendations", 2015; and other documents related to the movie CAKE: MNK-T1_0000877315; MNK-T1_0003009170; MNK-T1_0005976168; MNK-T1_0006038109; MNK-T1_0007066451.

science is appealing to prescribers because it provides a seemingly unbiased, non-commercial basis for the use of medication. The desire to integrate marketing messages with science is the foundation of many of the marketing strategies used by the Defendants.

54. Pharmaceutical marketers' interest in physician decision-making has motivated research on the impact of promotion on physician beliefs, knowledge, and self-reported behavior.[71] Avorn analyzed physician beliefs about the sources of influence on their prescribing. In this work, physicians were asked to report their beliefs about the pharmacologic effects of two classes of drugs where the scientific evidence had clearly shown little or no benefit while the manufacturers had advertised heavily to promote the drugs as superior to the therapeutic alternatives. Although the physicians reported that commercial sources of information had little influence on their prescribing habits, the majority held beliefs about the two classes of drugs that were consistent with the detailing message and at odds with the scientific evidence.[72]

55. However, when asked, physicians deny that gifts and payments could influence their prescribing behavior.[73] In fact, receipt of gifts from the industry was associated with the belief that pharmaceutical representatives have no impact on prescribing behavior.[74] Further, there is also evidence that there is a correlation between financial relationships between doctors and drug

[71] See e.g., E. Clayton, "'Tis Always the Season for Giving," CALPIRG Report, September 2004, pp. 1-9; Editorial Staff, "Pharmaceutical Marketing to Physicians: Free Gifts Carry a High Price," *American Medical News*, June 10, 2002; A. Wazana, "Physicians and the Pharmaceutical Industry," *The Journal of the American Medical Association,* 283(3), January 19, 2000, pp. 373-80; A. Fugh-Berman, "The Corporate Coauthor," *Journal of General Internal Medicine,* 20(6), June 2005, pp. 546-48.

[72] J. Avorn, M. Chen, and R. Hartley, "Scientific Versus Commercial Sources of Influence on the Prescribing Behavior of Physicians," *American Journal of Medicine,* 73(1), July 1982, pp. 4-8.

[73] A. Wazana, *op. cit*. See also J. Dana and G. Loewenstein, "A Social Science Perspective on Gifts to Physicians From Industry," *The Journal of the American Medical Association*, 290(2), July 9, 2003, pp. 252-55. Physician denial of the influence of industry communication, samples, and gifts (including free medical education) may be understood in the context of extensive findings from behavioral psychology regarding unintentional and subconscious biases.

[74] W. Sandberg *et al*., "The Effect of Educational Gifts from Pharmaceutical Firms on Medical Students' Recall of Company Names or Products," *Academic Medicine*, 72(10), October 1997, pp. 916-18; B. Hodges, "Interactions with the Pharmaceutical Industry: Experiences and Attitudes of Psychiatry Residents, Interns and Clerks," *Canadian Medical Association Journal,* 153(5), September 1, 1995, pp. 553-59.

companies: greater payments relating to higher volumes of the brand name drugs being prescribed.[75]

56. For example, Hadland et al. (2018) examined the association between pharmaceutical industry marketing of opioids and subsequent physician opioid prescribing behavior. This research, using the Open Payments and Medicare Part D Opioid Prescriber Summary File, analyzed the extent to which pharmaceutical industry marketing of opioids to physicians during 2014 was associated with opioid prescribing behavior during 2015. The results indicated that "receipt of any opioid-related payments from industry in 2014 was associated with 9.3% (95% CI, 8.7%-9.9%) more opioid claims in 2015 compared with physicians who received no such payments…" (p. 862). Hadland also investigated the impact of industry meals provided to physicians finding that "each additional meal was associated with an increase of 0.7% (95% CI, 0.6%-0.8%) in opioid claims."[76]

57. Other research has supported the growing concerns over payments from drug makers to prescribers.[77] [78] This body of literature suggests that regardless of what prescribers may think

[75] Charles Ornstein, Mike Tigas and Ryann Grochowski Jones. Dollars for Doctors, Now There's Proof: Docs Who Get Company Cash Tend to Prescribe More Brand-Name Meds. ProPublica, March 17, 2016. https://www.propublica.org/article/doctors-who-take-company-cash-tend-to-prescribe-more-brand-name-drugs (last accessed March 2, 2019). See working paper methodology: https://static.propublica.org/projects/d4d/20160317-matching-industry-payments.pdf?22 (last accessed March 9, 2019).

[76] Hadland S, Yu L, Krieger M, Marshall B and Cerda M. Association of Pharmaceutical Industry Marketing of Opioid Products to Physicians with Subsequent Opioid Prescribing. JAMA Internal Medicine, June 2018; 178(6):861-863.

[77] Zezza M and Bachhuber M. Payments from drug companies to physicians are associated with higher volume and more expensive opioid analgesic prescribing. PLOS|ONE December 19, 2018. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0209383 (last accessed February 20, 2019).

[78] Mitchell A, Winn A, Lund J, and Dusetzina S. Evaluating the Strength of the Association Between Industry Payments and Prescribing Practices in Oncology. The Oncologist. Online: February 6, 2019. http://theoncologist.alphamedpress.org/content/early/2019/01/31/theoncologist.2018-0423 (last accessed February 9, 2019); Grande D. Limiting the influence of pharmaceutical industry gifts on physicians: self-regulation or government intervention? J Gen Intern Med. 2010;25(1):79-83; Greenland P. Time for the medical profession to act: new policies needed now on interactions between pharmaceutical companies and physicians. Arch Intern Med. 2009;169(9):829-831; Yeh JS, Franklin JM, Avorn J, Landon J, Kesselheim AS. Association of industry payments to physicians with the prescribing of brand-name statins in Massachusetts. JAMA Intern Med. 2016;176(6):763-768.

about their decision-making, and the inputs to the decision-making process, the role of the pharmaceutical marketer significantly impacts their prescribing.[79]

Personal Selling

58. Prescribers need to continually educate themselves about drugs to determine which are best. They therefore rely on pharmaceutical companies as a source of needed drug information.[80] Pharmaceutical companies use pharmaceutical sales representatives (PSRs) to provide information to prescribers and to generate prescriptions.[81] In fact, personal selling, also referred to as product detailing, through PSRs and medical science liaisons (MSLs), is effective and consistently accounts for more than half of all pharmaceutical marketing expenditures industry-

[79] See e.g., Grande D. Limiting the influence of pharmaceutical industry gifts on physicians: self-regulation or government intervention? J Gen Intern Med. 2010;25(1):79-83; Greenland P. Time for the medical profession to act: new policies needed now on interactions between pharmaceutical companies and physicians. Arch Intern Med. 2009;169(9):829-831; Hadland S, Yu L, Krieger M, Marshall B, and Cerda M. Association of Pharmaceutical Industry Marketing of Opioid Products to Physicians with Subsequent Opioid Prescribing. JAMA Internal Medicine, June 2018; 178(6):861-863; Zezza M and Bachhuber M. Payments from drug companies to physicians are associated with higher volume and more expensive opioid analgesic prescribing. PLOS|ONE December 19, 2018, https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0209383 (last accessed February 20, 2019); Orlowski JP and Wateska L. The Effects of Pharmaceutical Firm Enticements on Physician Prescribing Patterns. CHEST 1992; 102(1):270-273; Mitchell A, Winn A, Lund J, and Dusetzina S. Evaluating the Strength of the Association Between Industry Payments and Prescribing Practices in Oncology. The Oncologist. Published online before print February 6, 2019. http://theoncologist.alphamedpress.org/content/early/2019/01/31/theoncologist.2018-0423 (last accessed February 9, 2019).

[80] I hold this opinion based on my experience and this is also supported by Defendants' testimony, e.g., Jolliff_MNK Deposition pp.174-175; Bingol, Demir_Endo Deposition, pp.199-200 and Endo-Bingol-016; Condodina, Cynthia_Teva Deposition, pp.257-258; Cox, Erin_MNK Deposition, pp.87-88. Note this testimony states that "[physicians] would never rely on me" while at the same time indicating that physicians expected "accurate information."

[81] See e.g., Ali Murshid M, Mohaidin Z. Models and theories of prescribing decisions: A review and suggested a new model. Pharmacy Practice 2017 Apr-Jun;15(2):990; Datta A and Dave D. Effects of Physician-directed Pharmaceutical Promotion on Prescription Behaviors: Longitudinal Evidence. Health Economics. April 2017;26(4):450-469; Stros M and Lee N. Marketing dimensions in the prescription pharmaceutical industry: a systematic literature review. J of Strategic Marketing 2015;23(4):318-336.

wide.[82] [83] [84] PSRs generally create notes, referred to as "call notes," that may partially document a PSRs interaction with Customers.[85]

59. Defendants' marketing recognized the value of personal selling. For example, in a marketing presentation at ENDO, prepared by ZS Associates (a commercial marketing research and support company), it was noted with respect to the pain portfolio, *"Sales force detailing is the most impactful tactic, detailing accounts for ~35-65% of all sales and marketing impact."*[86] Further recognizing the need and value for personal selling efforts in order to maintain sales, Janssen contracted with Quintiles for approximately $24 million ($12 million per year for two years) when its Nucynta IR and ER sales force were transitioned to other drugs.[87]

60. MSLs, while not classified as sales personnel, contribute to sales effectiveness through their contributions to marketing intelligence as well as Customer education. For example, Allergan

[82] See e.g., Creyer E and Hrsistodoulakis I. Marketing pharmaceutical products to physicians: sales reps influence physicians' impressions of the industry. Marketing Health Services. 1998; 18(2): 34-38; Huston P. Doctors want more industry-sponsored meetings. Medical Marketing & Media. 1993; 28(3): 48-53; John Mack, Pharma Marketing News. Pharma Promotional Spending in 2013. http://www.pharma-mkting.com/news/pmnews1305-article01.pdf (last accessed August 13, 2018); Anon. Persuading the Prescribers: Pharmaceutical Marketing and its Influence on Physicians and Patients. (last accessed November 11, 2013). http://www.pewtrusts.org/en/research-and-analysis/fact-sheets/2013/11/11/persuading-the-prescribers-pharmaceutical-industry-marketing-and-its-influence-on-physicians-and-patients (last accessed August 13, 2018); Gonul, F., Carter, F., Petrova, E., & Srinivasan, K. (2001). Promotion of prescription drugs and its impact on physicians' choice behavior. Journal of Marketing, 65, 79–90.

[83] For Purdue, in about 2004, the cost of a sales presentation by a PSR was estimated at $134. With a sales force of 550 PSRs, the company estimated its daily cost of sales calls to be $73,700. PPLPC029000132250, Sales Force Metrics, p.6.

[84] The sales force is recognized in the industry to impact sales, in fact, the larger the sales force, the greater the top-line sales expectations. See e.g., Teva Trial Day 3, Gasdia – direct. Mr. Gasdia provides testimony regarding sales force effectiveness in increasing OxyContin sales, pp.76-78; 39_MNK-T1_0000228064 p.42; ENDO-CHI-LIT-00214471, p.8; Actiq 2002 Marketing Plan, TEVA_MDL_A_00454816. See also, e.g., Pennsaid Strategic Imperatives, MNK-T1_0000126893, p.23,29,37; Exalgo Message Recall Research, MNK-T1_0000185447, p.5.

[85] See Schedule 12: Manufacturing Defendant Call Notes and Schedule 13: Cuyahoga County and Summit County Call Notes.

[86] Endo Promotional Mix Optimization Brand Level Model Results and ROI, ENDO-CHI_Lit00214471.

[87] JAN-MS-01049919; JAN-MS-00576727 Lin_Janssen Deposition Exhibit 11. This contract provided 77 PSR along with seven District Managers and a Project Leader.

MSLs collected marketing intelligence at an American Pain Society meeting focused on the potential dangers of opioid use.[88] Ms. Barrett, who was for a time a Medical Affairs employee at Allergan, stated that MSLs *"…always go with a purpose for covering the pain society meetings. So it's an opportunity to understand cutting edge science. It's an opportunity to understand what's going on with competitors, treatment paradigms, guidelines, all those kinds of things."*[89]

61. Personal selling is one of the most powerful and widely used pharmaceutical marketing techniques. Defendants' marketing documents and the research and practical literature support this proposition.[90] [91] Personal selling is effective because it utilizes both information and "relationship building" to communicate with, educate, and influence the prescriber.[92] Further, sales personnel can directly provide promotional materials that reinforce sales messages even after a sales call.[93] However, recipients of marketing materials provided by pharmaceutical companies should use this information for medical decision-making carefully as it is may not always be accurate.[94] [95]

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[88] Email and slide presentation regarding posters presentations at a 2012 APS meeting. MSLs are collecting marketing intelligence on Allergan and competing products. This information is made available to the sales force. Allergan_MDL_00459147. This and similar meetings also underscore the valuable role Advocacy groups (discussed below) played for Defendants.

[89] Barrett_Allergan Deposition, pp.115-116.

[90] Campo K, Staebel OD, Gijsbrechts E, and Waterschoot W. Physicians' Decision Process for Drug Prescription and the Impact of Pharmaceutical Marketing Mix Instruments. Health Marketing Quarterly 2005;22(4):73-107; Orlowski JP and Wateska L. The Effects of Pharmaceutical Firm Enticements on Physician Prescribing Patterns. CHEST 1992;102(1):270-273.

[91] See e.g., Actavis. Inventiv Sales Training, May 20 2009. ACTAVIS-581557 p9 where the impact of reduction in detailing volume over time is expected to decline.

[92] Manchanda P, Honka E. The effects and role of direct-to-physician marketing in the pharmaceutical industry: an integrative review. Yale J. Health Policy Law & Ethics 2005;5:785-812.

[93] M.Y. Peay and E.R. Peay. The Role of Commercial Sources in the Adoption of a New Drug. Social Science and Medicine 1998; 26:1183–1189.

[94] Cardarelli R, Licciardone JC, Taylor LG. A cross-sectional evidence-based review of pharmaceutical promotional marketing brochures and their underlying studies: is what they tell us important and true? BMC Family Practice 2006;7:13; Cooper RJ, Schriger DL, Wallace RC, Mikulich VJ, Wilkes MS. The Quantity and Quality of Scientific Graphs in Pharmaceutical Advertisements. Journal of General Internal Medicine, 2003;18:294-297; Villanueva P, Peiro S, Librero J, Pereiro I. Accuracy of Pharmaceutical Advertisements in Medical Journals. Lancet 2003;361:27-32.

[95] Pfyer_Teva Deposition 18 (2002 Actiq Marketing Plan); Beckhardt.Stacey.Teva.2.1.2019 Deposition, pp.230-232, 250-256, 459-460 and Exhibit 14.

62. Finally, personal selling and relationships in marketing are complex and physicians are reluctant to acknowledge the impact that personal selling and other forms of pharmaceutical promotion may have on their prescribing practices.[96] Indeed, physicians may not be able to easily discriminate between promotional information and scientific evidence[97] and further believe that their colleagues are more susceptible to industry influences than themselves.[98]

63. Yet, prescribers need accurate drug information to take good care of their patients. When there is an information need, a virtual army of PSRs stands ready to step in and provide the information and messages created by their companies. The information and education provided by PSRs is marketing. Marketing at its core has the goal of increasing product awareness and knowledge by providing information to customers. This information educates customers, but is marketing, nevertheless. Manufacturers, including Defendants which compensated PSRs based on incentives, confirm this by attaching financial rewards to the education PSRs provide and the outcomes of that education: prescription sales.[99]

[96] Chimonas S, Brennan TA, Rothman DJ. Physicians and drug representatives: exploring the dynamics of the relationship. J Gen Intern Medicine 2007;22:184-190.

[97] Fickweiler F, Fickweiler W, Urbach E. Interactions between physicians and the pharmaceutical industry generally and sales representatives specifically and their association with physicians' attitudes and prescribing habits: a systematic review. BMJ Open 2017;7:e016408.

[98] Patwardhan A. Physicians-Pharmaceutical Sales Representative Interactions and Conflict of Interest. Inquiry 2016; 53:1-5.

[99] See e.g., Dorsey, Michael_Allergan, pp.54-62; Becker.Kevin.MNK Deposition, pp.121-122; Bingol, Demir_Endo Deposition, p.276; Boothe, Douglas_Allergan Deposition, pp.36-40; Hassler_Teva 30(b)(6) Deposition, pp.247-248; Adams.John.MNK Deposition, pp.88-89; Becker, S_MNK Deposition, pp.52-53; Chick, S_MNK Deposition, pp.170-171; Condolina_Teva Deposition, p.162; Cramer, Phil 11-20-18 Deposition, pp.173.174; Day, Matthew_Teva Deposition, pp.117-118; Dumont, Kirk_MNK pp.27-28; Gillenkirk, Corine_Teva Deposition, pp.27-28, 254; Lin, D_Janssen Deposition, pp.253-254; Neely, Kate_MNK Deposition, pp.17-18; Perfetto, M_Allergan Deposition, pp.311-312; Romaine, Larry_Endo Deposition, pp.117-119; Snyder_Allergan Deposition, pp.159-160 and Exhibit 5; Kilper, Jeffrey,MKN.2.6.2019, pp.90-104; Deem_Eshleman_Janssen Deposition, p.189; Jim Lang memo to Russ Gasdia and Mike Innuurato, regarding Abbott, December 4, 2000 (PKY181173153).

Research, Publications & Medical Journal Advertising

64. Medical journals are useful to the pharmaceutical marketer because they contain published research and advertising. Peer-reviewed publications are generally considered to be unbiased and reliable sources of information, and physicians rely on the conclusions of research studies to make decisions for their patients. Azoulay investigated the impact of both pharmaceutical company promotional efforts and scientific publications on prescribing behavior for anti-ulcer drugs and found a significant effect on sales for both types of communication.[100] This preference for science-based information is foundational to many of the Defendants' pharmaceutical marketing activities identified in this Report.

65. However, the ever-increasing volume of research and publications may contain commercial bias because of the prevalence of company-sponsored[101] research for the drug under evaluation.[102] [103] Even so, peer-reviewed research, with appropriate disclosures of funding sources and investigators' potential conflicts of interest, may still be perceived by prescribers as unbiased. When commercial interests are not disclosed or are disguised, and conflicts are perceived or are discovered, the credibility of the information in the publication is diminished.[104]

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[100] P. Azoulay, "Do Pharmaceutical Sales Respond to Scientific Evidence?" *Journal of Economics and Management Strategy*, 2002; 11(4):pp.551-94. It should be noted that because many scientific studies of prescription drugs are funded by the manufacturer the separation between promotion and scientific evidence that Azoulay assumes may not truly exist.

[101] Company sponsored research can include financial or other support provided in the conduct of research or in the publication process. This would include, for example, research funding, study protocol development (research design, clinical endpoints, study period, etc.), writing assistance, payments to investigators who may also be KOLs or provide other paid consulting services (e.g., CME talks) to companies.

[102] See e.g., Tasi A. Conflicts Between Commercial and Scientific Interests in Pharmaceutical Advertising for Medical Journals. International Journal of Health Services Research, 2003; 33(4);751-768; L. Friedman and E. Richter, "Relationship Between Conflicts of Interest and Research Results," *Journal of General Internal Medicine*, 2004; 19(1):51-56.

[103] See e.g., Publication Plans, ENDO-CHI_LIT-00551008; Bingol, Demir_Endo Deposition, pp.81-83.

[104] See e.g., Cooper R and Schriger D. The availability of references and the sponsorship of original research cited in pharmaceutical advertisements. Canadian Medical Association Journal, 2005; 172(4):487-491; Friedman L and Richter E. Relationship Between Conflicts of Interest and Research Results. Journal General Internal Medicine 2004; 19(1):51-56.

66. Pharmaceutical marketers also advertise in medical journals, alongside peer-reviewed research.[105] This advertising works because when prescribers are reading medical journals and the research contained therein, they also see promotional, company-sponsored advertisements. The presence of advertisements, alongside credible research tends to lend credibility to the advertisements, making them more effective.[106]

Peer-to-Peer Marketing

67. A core marketing principle is opinion leadership, because people listen to others whom they believe have greater knowledge and experience about a subject. A significant driver of a physician's view of a drug is how the drug is perceived by peer-physicians, making "opinion leadership" or "peer-to-peer" marketing an effective sales technique. Peer-to-peer marketing uses key opinion leaders (KOLs) or "influencers" and word-of-mouth to create an expanding awareness and more rapid adoption of new pharmaceuticals by prescribers and other stakeholders. Using KOLs can legitimize marketing messages, increase product awareness, and

[105] See e.g., advertisements run in medical journals with distribution in Ohio including: Vicodin HP and Ultram in American Family Physician, January 1997; Oxycontin and Duract, American Family Physician, September 1997; a Pain Care Coalition (AAPM, APS are part of this group, their role with Defendants is addressed below) public service ad for responsible pain care, Headache, March 1999; OxyContin, NEJM, May 2000; Duragesic and Hydromorph Contin and the non-branded Janssen ad for ElderCare, American Geriatrics Society, April 2002; OxyContin, JAMA, November 2002; Xytrel XL, Canadian Medical Association Journal, April 2007. See also, journals which published articles on pain, opioids and addiction, including e.g., CMAJ, Archives of Internal Medicine, The Lancet, Pain, Headache, Journal of Family Practice, Journal of Pain, JAMA and NEJM between about 1997 and 2010.

[106] Fugh-Berman A, Alladin K and Chow J. Advertising in Medical Journals: Should Current Practices Change? PLoS Medicine, 2006; 3(6):e130. https://journals.plos.org/plosmedicine/article/file?id=10.1371/journal.pmed.0030130&type=printable (last accessed December 9, 2018).

convey favorable impressions and experience with a drug.[107] Mr. Bingol, a Senior Marketing Director at Endo, explained the benefit of using KOLs:[108]

Q. Okay. Next bullet point discusses engage KOL to legitimatize messages. Is that a reference to what we discussed earlier in terms of your use of KOLs in connection with the promotion of Opana ER?

MR. LIMBACHER: Object to form.

A. Using KOLs as thought leaders -- they had a broad network and a broad following, and if they were -- as they work with you, it brings more credibility to the message.

Q. (By Ms. Scullion) So that could help legitimatize the message that Endo wanted to send to the market about Opana ER, for example?

A. It would help legitimatize the need and the utility of our product in those appropriate patients.

Q. It would also help legitimatize the message; correct?

MR. LIMBACHER: Object to form

A. That is the message, that for patients who are undertreated or not be able to get the pain relief they made with the adverse event profile they might be able to tolerate, that there's another option.

[107] See generally, e.g., Leveraging Peer-to-Peer Networks in Pharmaceutical Marketing. Innovation & Marketing in the Pharmaceutical Industry, Emerging Practices, Research, and Policies. Ding, Eliashberg and Stremersch Eds., Springer, 2014, Chapter 15, p.457-475; David Rear, Show Me the Money, Medical Marketing & Media, May 2012, mmm-online.com, Med Ed Report 2012 pp.52-54; J.S. Coleman, E. Katz, and H. Menzel. Social Processes in Physicians' Adoption of a New Drug. J of Chronic Diseases, 1959;9(1):1-19; E.R. Berndt, R.S. Pindyck and P. Azoulay, "Consumption Externalities and Diffusion in Pharmaceutical Markets: Antiulcer Drugs," The Journal of Industrial Economics, 2003; 51(2):243-270.

[108] Bingol, Demir_Endo Deposition, p.95.

68. Another benefit of peer-to-peer marketing is the expansion of the marketer's "reach." Because some physicians refuse to see PSRs, peer-to-peer marketing enables manufacturers to pass messages along to these physicians who may not be reachable via personal selling. Further, peer-to-peer networks increase efficiency and return on investment (ROI) when used synergistically with the sales call, as targeted prescribers are reached via both the sales encounter and through social and professional networks.[109] Similarly, some companies have employed the use of industry advisory boards, bringing KOLs and others together to discuss drug issues, the marketplace and individual experiences.[110] By engaging KOLs, manufacturers tap into a critical antecedent for a prescription drug: the experience of peers and the confidence this brings to the decision process. As Endo co-founder and former CEO Carol Ammon explained, "thought leaders" "would not only talk about [a company's] products but would really start to move the whole market towards a change in pain management."[111] However, because KOLs are cultivated by pharmaceutical companies interested in advancing their drugs, the objectivity of KOLs may be questioned.[112] [113] [114]

[109] Leveraging Peer-to-Peer Networks in Pharmaceutical Marketing. Innovation & Marketing in the Pharmaceutical Industry, Emerging Practices, Research, and Policies. Ding, Eliashberg and Stremersch Eds., Springer, 2014, Chapter 15, p.457-475.

[110] See e.g., Opana ER National Advisory Board, ENDO-CHI_LIT-00034272; ENDO-CHI_LIT-00210619; INSYS, Advisory Board January 19, 2013, INSYS-MDL-000104814; MNK-T1_0000206953; JAN-MS-00304927; JAN-MS-0043627; MNK-T1_0000108564; MNK-T1_0000117600; INSYS-MDL-000468611; PPLP003400564, National Pain Advisory Meeting, Purdue Pharma; ACTAVIS0403159, Actavis Moxduo Advisory Board Report.

[111] https://www.youtube.com/watch?v=6fqFOy-bZ1k&t=258s (last accessed March 11, 2019); Bingol, Demir_Endo Deposition, p.95.

[112] See e.g., D'Arcy E. Presence, alignments and shared authenticity: Considering the new era of engagement between experts and the pharmaceutical industry. Journal of Medical Marketing 2009; 9(2):175-183; Elliott C. The Secret Lives of Big Pharma's 'Thought Leaders." Chronicle of Higher Education 2010; 57(4); Moynihan R. Key Opinion Leaders Independent Experts or drug representatives in disguise? British Medical Journal 2008; 336(June):1402-1403; Iskozitz M. MD Twitter-base may help ID KOLs. Med Ed Report, mmm-online.com December 2012, Medical Marketing and Media, p.23; Mack J, Developing Win-Win Key Opinion Leader Relationships. Pharma Marketing News 2003; 2(10):3-5. Available at: http://www.news.pharma-mkting.com/pmn210-article01.pdf (last accessed January 3, 2019).

[113] See e.g., PPLPC025000005629, Email between Dr. Portenoy and David Haddox (Purdue) regarding an educational conference they attended. Haddox is impressed by Portenoy's agenda and will help to shepherd Purdue grant dollars to Dr. Portenoy at Beth Israel Medical Center (BIMC). Portenoy responds:

69. An advisory board brings together multiple opinion leaders where topics related to the drug, disease, indications, side effects, or other issues are openly discussed. Through this process, a

"thanks also for keeping us in mind when you succeed in springing some funds for the absolutely critical work that has to be done by PF and others on the issues we talked about. Just yesterday, I was at a meeting of BIMC bigwigs and told the story (again) of how PF helped change the world a decade ago in terms of cancer pain management…"; PPLPC025000005743, Email from Robin Rosenbluth, Director of Development at BIMC to David Haddox (Purdue), attaching information about the Project on Pain and Chemical Dependency, and expressing gratitude for Haddox's efforts to "secure philanthropic support" for the program. "[W]onderful to discover that you are a crusader with a mission, like Russ Portenoy, committed to changing the thinking in the field about pain medicine and the chemically dependent. I am pleased to attach a write-up about the Project on Pain and Chemical Dependency."; PPLPC025000005759, Email exchange between Dr. Portenoy and David Haddox regarding Purdue funding for an upcoming pain project. Reference is made to Janssen and funding from other companies are also mentioned; PPLPC020000005715, Email by Dr. Portenoy, requesting identification of physicians against use of opioids for non-cancer patients for a television broadcast, with Haddox identifying a few that are against, but still in-line with their general agenda of pseudoaddiction, and distinction between physical dependence versus addiction.; PPLPC025000011326, Email exchange between Dr. Portenoy and David Haddox asking Dr. Portenoy to speak at a Purdue Opioids dinner symposium.; END00374834, Email from Winifred Schein, Director of Development, Dept of Pain Medicine & Palliative Care at BIMC submitting an invoice to Endo for the "Opioid Rotation Project" which was "generously supported by Endo."; PPLP004025432, email exchange between Dr. Portenoy and David Haddox regarding an article stating that Purdue was advocating for opioid use on infants. Haddox sent the article link to Dr. Portenoy, who then responded to the journalist, "remember the millions with poorly controlled pain as you pursue your advocacy agenda"; PPLPC025000019244, Email from Dr. Steve Passik to David Haddox copied to Dr. Portenoy regarding "expansion of [Dr. Portenoy's] program on Pain and Chemical Dependency with Passik at the head of it – turning it into an ambitious clinical and research institute," necessitating industry backing and 1.5 million in funds, inquiring whether Purdue would be interested in funding; Other similar email correspondence on this point can be seen in PPLPC021000012126; JAN-MS-00784576; PPLPC027000014110; JAN-MS-00725920 (Duragesic, Molly McDonald); PDD1800012102; PKY182085214; PPLP004018042; ENDO-OPIOID_MDL-00996699; PPLP004347618; ENDO-OPIOID_MDL-01592486 (Email discussing supplemental grant requested by Dr. Portenoy for Endo funded Opioid Rotation Meeting.); JAN-MS-00392809 (Pain treatment in the ED); PPLP004358732; PPLP004354276; TEVA_MDL_A_07547524 Email from Arvind Narayana thanking Dr. Portenoy for his input on the Fentora Advisory Board, attaching an executive summary of the board, and requesting edits by Dr. Portenoy prior to further circulation; END00148765 Email from Linda Kitlinski, Senior Director of Clinical Affairs for Endo, inquiring about publication of a paper written by Portenoy and Fine re: Opioid Rotation, indicating that Endo owed a "final grant payment," and expressing eagerness to share the paper with Endo leadership.; TEVA_MDL_A_07559050; JAN-MS-00392825; JAN-MS-00929471; MNK-T1_0002145008 Email from Joanna Schooler the VP of Medical Affairs and CMO of Pharmaceuticals at Covidien, advising Dr. Portenoy that the FDA approved Exalgo Hydromorphone extended release, and thanking Dr. Portenoy for his support in Covidien's efforts.; TEVA_MDL_A_07027227; PPLP004016754; TEVA_MDL_A_07030364; TEVA_MDL_A_07030502 (advisory board); TEVA_MDL_A_03799210.

[114] Steinbrook R. Commercial support and continuing medical education N Engl J Med. 2005;352(6):534-5.

pharmaceutical manufacturer can glean significant market information, learn how its' drug is perceived in the medical community, and identify new strengths, weaknesses, opportunities, or threats. It also provides the opportunity for KOLs to exchange information that could impact their own prescribing practices. In sum, KOLs are used to "infect" other prescribers with favorable opinions regarding a company's drug.[115]

70. An extension of peer-to-peer marketing is the use of health advocacy groups, which often provide national level thought and policy leadership related to disease and treatments. Defendants were able to more widely disseminate their marketing messages, which had the added benefit of appearing to be unbiased, by supporting and influencing such advocacy groups.[116] This included the pain market in Ohio, which for Janssen was the second largest

[115] Altier_Allergan Deposition, p.183 and Exhibit 6.

[116]See e.g., PPLPC009000026013_Confidential, Purdue budgeting spreadsheet (drug by drug) allocating payments to numerous marketing activities, including advocacy groups (e.g., AAPM) ; PWG003927496, Consultant Services Agreement between Purdue and James Campbell; PPLP003364381, Grants to organizations, including American Academy of Pain Management and American Pain Society; PPLP003364382, Summary of Payments to entities January 1, 2012 through March 28, 2017, including American Pain Society and AAPM; ENDO-CHI_LIT-00247966, Excel file of payments made by Endo to organizations and individuals, including Perry Fine, Russell Portenoy, Scott Fishman, American Pain Foundation, American Academy of Pain Medicine, American Pain Society, JCAHO, Wisconsin Pain and Policy Study Group (Board of Regents of the University of Wisconsin - Unrestricted educational grant); JAN00118932, Educational Grant Agreement. Payee: American Pain Society; JAN-MS-00919438, American Pain Society Corporate Membership Brochure; ALLERGAN_MDL_01010175, Actavis employees discuss what level of APS corporate membership they are willing to pay for. Actavis needs "a clear plan with objectives for meeting with them." Corporate Circle costs $25,000 to join; EPI000648788, Endo Request form for Educational Grant Payment to APS; MNK-T1_0000856189, PKY180259180, Leadership Summit on Pain Management, supported by a grant provided by Purdue Pharma; MNK-T1_0000919107, Mallinckrodt excel sheet listing grant requests from various organizations, including American Pain Society; APS-MDL00000020, APS written Agreement for Commercial Support with ENDO; PPLPC021000246625, Purdue Grant Summary. Includes grants for APF, APS; JAN-MS-00000001- 1997-2011 List of Janssen payments made to various advocacy groups such as AAPM, AGS, APF, APS, JCAHO, Center for Bioethics and honorarium fees to KOLs such as Portenoy, Fishman, and Fine; PPLPC036000002057, email from Jim Guest to Richard Sackler, Robin Hogen, Haddox where J. Guest wrote "Jim Campbell and I are looking forward to our meeting with you on Monday" and thanked them "for the positive response and useful suggestions … on the American Pain Foundation's proposed "Stop Pain Now!" campaign." Guest noted APF "refined the campaign plan" by incorporating many of Purdue's suggestions and attached the "revised plan along with an executive summary." Attached to this email were SPN Proposal 8-3-00.doc (PPLPC036000002058) and SPN Exec Summary 8-3-00.doc (PPLPC036000002078), Pain as the Fifth Vital Sign.

Nucynta state account in the U.S.[117] Groups such as the American Pain Society, which advocated "Pain as the Fifth Vital Sign,"[118] sought to elevate awareness of pain and its treatment – a goal that is consistent with Defendants' marketing.[119] [120] [121]

71. Other groups such as, for example, the American Academy of Pain Medicine (AAPM), American Geriatrics Society, and the American Pain Foundation all worked to increase the awareness of and access to pain treatment.[122] In 1997, APS and AAPM issued a Consensus Statement that

[117] Update & 2013 National Advocacy Business Planning, JAN-MS-00393085. This document is specific to Ohio as well as the national level. It touts Purdue, Janssen, Pfizer, and Endo as providing the highest total advocacy support in 4 categories: programmatic support, capacity building, access, and reimbursement, and general support. The "Imagine the Possibilities Pain Coalition" included here maps out advocacy projects, objectives and timelines for dissemination. This coalition is "...a working group of recognized experts in the field of pain aiming to fill unmet needs and gaps in patient care." This definition is remarkably like the goal of marketing. On slide 16 is a compilation of representative organizations Janssen was committed to regarding pain advocacy.

[118] The American Academy of Pain Medicine ("AAPM") and the American Pain Society ("APS") are professional medical societies, each of which received funding from Defendants. In about 1996, the APS Trademarked "Pain is the 5th Vital Sign" advocating to elevate pain to the "fifth vital sign," along with temperature, pulse, respiration rate, and blood pressure. See also, e.g., SPN Exec Summary 8-3-00.doc (PPLPC036000002078), Pain as the Fifth Vital Sign; CHI_001715571, STOP PAIN NOW, A campaign to Make Effective Pain Relief a National Priority, A Proposal to Purdue Pharma Submitted by the American Pain Foundation, August 7, 2000 (Updated March 2001); PPLPC0170001258, David Haddox 2008 email with the subject Re: Story about prescription narcotic use.

[119] PKY181559213, Managing Pain in Patients with Addiction and the "fifth vital sign." PPLPC017000062602 - Purdue Pain Advocacy Tool Kit uses APS's "Pain: The 5th Vital Sign" as part of its marketing strategy and on page 10 quotes James Campbell's November 11, 1995 APS Presidential Address, "We need to train doctors and nurses to treat pain a vital sign."; ABT-MDL-KY-0043299 - Talking points/binder of information on Oxy. Includes: JCAHO Pain Standards for 2001 (p. 13 of 86 of the PDF), 1998 FSMB Model Guidelines for the Use of Controlled Substances for the Treatment of Pain (p. 25 of 86 of the PDF). The binder also cites The Fifth Vital Sign as a trademark of the APS (p. 39 of 86 of the PDF)).

[120] In JAN-MS-00383085, Janssen answers the question of how advocacy can have an impact for chronic pain and diabetic peripheral neuropathy: creating awareness of the disease, latest treatments and barriers to access, and improving and maintaining access by shaping policy, public and private outreach (e.g., letters of support from partner organizations) and impacting legislation.

[121] Mr. Bingol at Endo regarded the "tag line" of "pain as the fifth vital sign" as an opportunity on a "market-wide" basis. Bingol, Demir_Endo Deposition, pp.225-226. This supports the proposition that the marketing messages seen in this case benefited not only the company that initiated the message, but also other competitors.

[122] See e.g, PDD8801101275, Richard Sackler email to K. Foley and J. Campbell suggesting Purdue and APS could work together to "protect the gains made in recognizing and treating pain patients."; American Pain Foundation Board of Directors Meeting, March 26, 2001, Minutes (CHI_001260914, pp.3-4, selling

endorsed opioids to treat chronic pain and claimed, among other things, that pain is often managed inadequately and that commonly held assumptions about opioids need modification with respect to addiction, respiratory depression and other side effects, tolerance and diversion.[123] In 2001, AAPM disseminated a press release regarding diversion and abuse of controlled substances, which included the statement:[124]

> *"Experience and investigation have shown that when opioids are prescribed and used appropriately in the treatment of pain there is minimal danger of creating an addictive disorder. Evidence to date indicates that substance abuse problems have not increased as a result of the increased availability of therapeutic opioids. The public health problem represented by misuse of prescription opioids is miniscule in comparison with that of untreated and unrelenting pain."*

This press release expresses opinions that effectively minimized concerns over diversion and abuse. This and other positions held by advocacy groups which were consistent with Defendants' marketing messages, when considered with Defendants' support of these advocacy groups, supports the proposition that Defendants' financial support had marketing purpose.[125]

72. Advocacy support by Defendants also was extended to groups like the Joint Commission on Accreditation of Hospitals (JCAHO) and the Federation of State Medical Boards (FSMB) both of which distributed guidelines or standards for opioid use.[126] In some instances, Defendants'

Pain Actions Guides at a profit to corporations) and Haddox email with his edits to a "Patient Action Pamphlet", PPLPC013000057412.

[123] The Chair of the committee that issued the statement, Dr. J. David Haddox, was a KOL for Purdue and thereafter a Purdue employee. He was also a past AAPM President (1988) Other authors, including KOL Dr. Portenoy, similarly had connections to defendants. APS-MDL00000005 AAPM and APS Consensus Statement - Use of Opioids for the Treatment of Chronic Pain. Other KOLs who worked with Defendants also served as President of AAPM including Drs. Fishman (2005), Fine (2011), and Webster (2013). https://painmed.org/about/board/council-of-past-presidents (last accessed February 9, 2019); See also, AAPS Consensus Statement; AGS Guidelines; APF Treatment Options for People Living with Pain.

[124] February 16, 2001 AAPM Press Release, PPLPC039000033400.

[125] Cramer, Phil_Deposition, pp.149-252, where Mr. Cramer is questioned by Mr. Hoffman about Purdue's distribution of materials consistent with WHO, APS and FSMB guidelines. What is not discussed is Purdue's support of advocacy groups like these or the KOLs and other influencers who assisted in the creation of these guidelines.

[126] See e.g. PPLPC021000155726, Purdue memo on alliances with JCAHO; CHI_000463727 CME approved by AAPM and FSMB, Responsible Opioid Prescribing; PKY181079987, CME by Endo and JCAHO; PKY180516748, Purdue sponsored Talk on Pain Management Addressing the New JCAHO Standards; PKY180130001, Leadership Summit on Pain Management, Sponsored by Joint Commission and American

support went beyond financial support aimed at influencing messages and included direct contributions or edits to advocacy messages. For example, Dr. Haddox provided comments and edits to the Pain Action Pamphlet distributed by the American Pain Foundation[127] and Responsible Opioid Prescribing (FSMB).[128]

73. Further support for the proposition that Defendants used KOLs, peer-to-peer marketing, and advocacy groups to reach marketing goals is seen in interactions with Dr. Portenoy. Dr. Portenoy, a well-known and outspoken KOL, was an important component of the Defendants' influence with advocacy groups. His work with industry, and advocacy groups supported by industry, culminated in dissemination of the industry supported messages Defendants wanted communicated in the marketplace. These messages were consistent with Defendants' promotional marketing messages and had the marketing purpose of creating more favorable perceptions about opioids, removing barriers to opioid use, and stimulating sales.[129]

74. Ms. Pamela Bennett, who worked for the American Pain Foundation as a consultant and was hired by Purdue in 2001, worked to create an advocacy "army" to support Purdue's sales[130] and its desire to disseminate new paradigms about opioids in the marketplace.[131] Working under the title of Advocacy Director, Ms. Bennett worked to create the Pain Control Advocacy Toolkit

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Pain Society is a conference supported by an unrestricted educational grant provided by Purdue Pharma; PKY180259180, Leadership Summit on Pain Management, Sponsored by Joint Commission and American Pain Society is a conference supported by an unrestricted educational grant provided by Purdue Pharma; PKY180458955, PKY180481945, and PKY180483734 are Purdue sponsored talks on pain management and the new JCAHO requirements; PKY181101825, District Manager Action Sheet, coordination of JCAHO activities; PKY180547091, Joint Commission Corporate Sponsor Draft Letter of Agreement, Purdue agrees to become the sole Corporate Sponsor of the JCAHO for certain educational initiatives; PKY180547097, Joint Commission Corporate Sponsor Draft Letter of Agreement. See also, Schedule 17: Amounts Paid to Pain Advocacy Organizations and Professional Societies.

[127] See Must, Alan_AM031419 Deposition, pp.75-81 and Must Exhibit 10.

[128] PPLP004123624, Haddox cover email and PPLP004123626, Haddox edits for Responsible Opioid Prescribing.

[129] See Section III of this Report.

[130] Bennett, P 011619 Deposition, pp.188-189 and Exhibit 17, Advocacy: Giving Voice for the People with Pain.

[131] Bennett, P 011619 Deposition, pp.28-29, 156-159, 175-187.

which had the goal of providing "…patients, their healthcare providers, their caregivers, and other advocates simple tools to express a strong, organized voice in the media and powerful governmental circles –tools that will help ensure the case for pain management will be heard and acess to appropriate treatment will be rapidly improved."[132] The toolkit provided specific training for its intended audiences on issues including, why advocacy is important (and who it should come from), to various talking points, how to get messages out, rules for talking with reporters, key audiences, how to use a press kit, and other key issues. Training on how to talk with reporters included, for example, the advice to not repeat negative remarks in reporters' questions. It offers the advice, that if a reporter asks a question such as, "Is an addiction to painkillers the issue here?", the respondent should offer, "No, the real issue is whether appropriate therapy for thousands of patients is being threatened by criminals and chronic abusers." Reframing the issue from addiction to blaming the problem on criminals and chronic abusers was consistent with Purdue's desire to reshape how Customers thought about opioids.[133] While Ms. Bennett did not characterize these activities as marketing, the use of opinion leadership by Purdue and other Defendants in this fashion, is marketing.[134]

75. Defendants' support of advocacy groups was significant.[135] This monetary support, as with KOLs, created an unavoidable conflict of interest, calling into question the independence of advocacy organizations. As described in this Report, working with these groups was an integral part of Defendants' marketing. However, Ms. Deem-Eshleman, a marketing professional who worked

[132] Bennett, P 011619 Deposition Exhibit 15, Pain Control Advocacy Toolkit.

[133] Bennett, P 011619 Deposition, pp.153-160.

[134] In her deposition, Ms. Bennett was asked: *"Do you think that deploying advocates from your army into a state like Ohio to offer statements in response to an article that's going to be published in a local paper about OxyContin abuse – do you think that is marketing?* Her response was, "*I think – well, no*." She went on to say, "*I think it—I think it's offering people an opportunity to express their opinion."* While the action of expressing opinions may or may not be marketing, Purdue's coordination of the process to ensure, and influence exerted, over the opinions expressed, is marketing. (Bennett P 011619 Deposition, pp.262-263.)

[135] See e.g., PPLPC017000604922, Organizational Payments, 2002-2015; Consider also, payments to KOLs like Dr. Portenoy who worked with advocacy groups. See also, Schedule 18: Amounts paid to KOLs and Schedule 17: Amounts paid to Pain Advocacy Organization & Professional Societies.

on the Nucynta brand and was a corporate representative for Janssen, indicated the company worked with but did not promote its products through outside organizations such as, for example, the American Pain Foundation, the American Academy of Pain Management, or the American Academy of Pain Medicine. In her testimony, Ms. Deem-Eshleman relied on semantics to support her characterization of Janssen's involvement with these groups, referring to some of this involvement as "unbranded" marketing.[136] From a marketing perspective, Janssen's work with advocacy, referred to as outside organizations in this context, supports the proposition that Janssen marketed through these organizations.

Continuing Medical Education (CME)

76. Pharmaceutical companies support educational efforts and routinely refer to their marketing as education.[137] This includes accredited CME and non-certified education.[138] However, accredited CME and non-certified education have distinct differences. Accredited CME activities include those supported by drug companies but intended to be independent of promotional influence. Accredited CME activities are attractive to physicians because they must earn a certain number of hours of CME each year to continue licensure, which attracts prescribers to industry-sponsored, free, CME. KOLs may also be used to deliver CME programs, adding value to the

[136] Deem_Eshleman_Janssen Deposition, pp.57-123 where she is questioned about work with outside organizations, specific messaging, marketing materials, and campaigns such as "Smart Moves" and "Smart Choices" aimed at educating youth about appropriate pain management. What she fails to recognize is that Janssen supported KOLs and the outside organizations it worked with in the creation and distribution of materials consistent with its own marketing messages. In addition to other evidence of support for advocacy organizations and KOLs, see the American Pain Foundation record of corporate support for its activities from Defendants, including Janssen at APS-MDL00000001.

[137] Defendants sometimes prefer to call marketing activities education. This practice does not preclude the fact that education of Customers is marketing.

[138] Defendants' marketing plans cited throughout this Report detail CME efforts. See also, Schedule 8: Manufacturing Defendant Marketing Plans, presenting a chronological listing of many of these plans. Other documents provide insight into how Defendants worked in tandem to train and educate Customers about their products, see e.g., PPLP003427266 Key Opinion Leader Training, Xcenda (AmerisourceBergen Consulting Services); JAN-MS-00814133, Pain Policy Educational Initiative, April 7, 2008, Xcenda PRS Business Unit.

sponsorship by the drug company.[139] However, this added value comes at the expense of potential bias that may stem from the use of a KOL who may have financial ties to the pharmaceutical company.

77. Medical education can also take the form of promotional-education activities. However, non-certified, promotional education that is controlled by a manufacturer must present information that is consistent with the FDA-approved label.[140] Yet, pharmaceutical companies seem to prefer accredited CME, possibly due to the expectation of return on investment which is estimated to be $3.56 in increased sales for each dollar spent on accredited CME.[141]

78. There are standards for non-promotional, accredited CME such as those established by the Accreditation Council for Continuing Medical Education (ACCME).[142] These standards were created to ensure CME activities are independent, free of commercial bias, and not influenced by those with an economic interest in the CME content. In general, CME activities usually include:[143]

- Educational Materials (e.g., publications, clinical practice guidelines)
- Medical Education Conferences (e.g., symposia, lectures, workshops)
- Peer-to-Peer Education (e.g., meetings with providers at their practice site, thought or opinion leaders)

[139] KOLs paid, see e.g., ENDO-CHI_LIT-002175549.
[140] See e.g., APT – NIPC Dinner Dialogue, END00033272.
[141] Brody H. Pharmaceutical industry financial support for medical education: benefit, or undue influence? Journal of Law, Medicine, & Ethics 2009;37(3):451-460.
[142] Accreditation Council for Continuing Medical Education, http://www.accme.org.
[143] Mazmanian P and Davis D. Continuing Medical Education and the Physician as a Learner: Guide to the Evidence. JAMA 2002; 288(9):1057-1060.

79. Pharmaceutical companies can evaluate CME by assessing its impact on brand performance.[144] [145] Another basic method for assessing return on CME is to assess the numbers of participants attending a CME program. However, the value of CMEs as a marketing tool goes beyond these metrics and can include assessment of learning that occurred, the effectiveness of the presenters, or how the CME may impact practice and patient care. These evaluations provide useful information to marketers that can help shape future marketing activities.[146] Finally, CME is also a way to further peer-to-peer education when participants interact and influencers (KOLs) are employed to provide educational programs.[147]

Clinical Practice Guidelines

80. Clinical practice guidelines (CPGs), sometimes referred to as clinical protocols or clinical pathways, are documents that contain structured recommendations designed to assist health care professionals in providing patient care. These guidelines seek to improve the process of care and patient outcomes and include decision aids in the selection of drug therapy.[148] Guidelines may be developed by institutions, researchers, advocacy groups, clinicians and others to provide evidence-based protocols for treatment. As noted above, Defendants used CPGs developed by KOLs and advocacy groups to perpetuate guidelines consistent with their marketing messages.

[144] See e.g., END00717275, Opana tactical plan with the success metric of brand performance pre-post educational programs.

[145] M. Chren and C. Landefeld, "Physicians' Behavior and Their Interactions With Drug Companies: A Controlled Study of Physicians Who Requested Additions to a Hospital Drug Formulary," *The Journal of the American Medical Association*, 1994; 271(19):684-689.

[146] Opana Tactical Plan 2012, END00717275 p.19; See also, related to speaker programs: MNK-T10001553091, noting increased speaker programs equates to more prescriptions and more bonus.

[147] See e.g., Beckhardt_Teva Deposition, pp.234-236; Condolina_Teva Deposition, pp.378-387; Vitanza_Endo Deposition, pp.262-264, with respect to CME included in an Opana RiskMAP (Exhibit 26); Vorsanger_Janssen_Vol 1, p.255.

[148] Graham R. Clinical Practice Guidelines We Can Trust. Washington D.C., National Academies Press, 2011.

81. Pharmaceutical marketers have recognized that influencing the development of clinical guidelines and ensuring the dissemination of favorable guidelines can have a significant impact on which drugs prescribers select, and therefore sales of drugs.[149] CPGs impact prescribing in the same manner as formularies: when a guideline drug is positioned as a first-line therapy, prescribers are more likely to prescribe the drug.

82. Defendants worked with KOLs and advocacy in the development of CPGs which was a part of Defendants' marketing. While effective for generating sales, the use of KOLs and advocacy organizations that are financially tied to Defendants creates commercial bias that can become part of the CPGs developed. (See Schedules 17 & 18) A good example of the close relationships between KOLs and advocacy groups is seen, for example, in activities associated with the book, Responsible Opioid Prescribing by Dr. Fishman. This text is referred to by the Federation of State Medical Boards (FSMBs) as the *"result"* of FSMBs *"Model Policy for the Use of Controlled Substance for the Treatment of Pain"* which was supported by Defendants. Fishman was a prominent KOL. The Fishman book was distributed to nearly 162,000 physicians and other prescribers through accredited CME.[150] Reshaping the minds of prescribers through CPG development and associated distribution of these guidelines through educational (marketing) activities was an important aspect of Defendants marketing because of the impact it could have on sales.[151]

[149] Choudhry Nm Stekfox H and Detsky A. Relationships between Authors and Clinical Practice Guidelines and the Pharmaceutical Industry. JAMA, 2002; 287(5):612-617; Detsky, Editorial, *Sources of bias for authors of clinical practice guidelines*, Canadian Medical Association Journal, 2006; 175(9):1033; Shaneyfelt T and Centor R. Reassessment of Clinical Practice Guidelines. JAMA 2009; 301(8):868-869.

[150] CAH_MDL2804_00846989. Email chain with a CE City proposal where Jonathan Jagoda, Policy and Government Relations Associate at the Federation of State Medical Boards notes the FSMB policy, Fishman text and past distribution.

[151] CPGs are generally perceived as unbiased giving these guidelines credibility. Further, prescribers concerned with liability feel more secure when prescribing based on accepted protocols and recommendations contained in CPGs. This gives CPGs the ability to significantly impact prescribing.

Influence on Formularies

83. Prescribing choices are influenced by which drugs are included on prescription formularies for insurance coverage.[152] When formulary drugs differ from prescribers' habits, prescribers must adapt their medication choices to match a patient's formulary, or the patient may have higher out-of-pocket costs or be denied coverage. This ties formulary decisions by the TPP or PBM to the success of a branded drug[153] and creates opportunities for pharmaceutical marketers who can effectively impact formulary decision-making. The record in this case supports the proposition that Defendants recognized and acted on the need to monitor and maintain the desired formulary status for their drugs.[154]

[152] *See* e.g., *Pharmaceutical Marketing*, Ch. 4 & 12, Rollins, B.L. & Perri, M. (eds.) (2013); Virabhak S., Shinogle JA. Physicians' prescribing responses to a restricted formulary: the impact of Medicaid preferred drug lists in Illinois and Louisiana. Am J of Managed Care 2005;11:SP14-20. https://europepmc.org/abstract/med/15700905.

[153] In most cases, generic products receive automatic, preferred tier status.

[154] See e.g., Managed Markets Formulary Mechanisms to Contain Costs, TEVA_CHI-00004939; Fully integrated marketing. ENDO-CHI-_LIT-00546731; PPLPC012000064369, Business Plan written by Bernie Katsur, Purdue National Account Executive; PPLPC018000199014, Draft script/outline for presentation on the U.S. healthcare system for HCPs, caregivers, and patient advocacy groups; PPLPC013000295860, Preponderance Clauses in negotiating Purdue commercial contracts for OxyContin and Butrans; PPLPC012000293223, Comprehensive pricing study and recommendations regarding formulary placement and rebates; PPLPC015000256864, Marketing report targeting long term care facilities, expected market share losses; PPLPC018000310455 – Email chain re: development of sales force training materials re: overcoming physician objections to prescribing drugs with unfavorable formulary status; JAN-OH-00005831, Field Coach Report, coupons and rebate cards; PPLPC019000043806 – Managers Meeting presentation, OxyContin rebates; PPLPC018001107461, pricing recommendations including weighted average cost, insurance reimbursement, and managed care limits and PPLPC018001096229, which is the appendix to this document with detailed data and analysis supporting pricing recommendations; PPLPC018000063433, "Proposed Rebates," Purdue planned to offer higher rebates to more restrictive "highly managed" formularies; PPLP003538597, Purdue Butrans Marketing Overview at slides 5,6,13,29,56; PPLP003516702, Purdue sales force memo: "Prior to this formulary win, patients who were classified as LIS/Dual Eligible had a strict PA in place requiring failure of ALL formulary options first. As of January 1, 2011, these patients have had access to OxyContin® for $2-$12." Also, "As a result of your efforts, Member Health/CCRx scripts have increased 34% since December 2010. However, the average TRx growth was 70% for the Districts utilizing the pull-through piece most often;" PKY182049869, market segment strategy for paradigm shift focused on pain management, ranking of segments; PPLP003523084, Purdue managed care sales training, "Push Up" (prescribers putting pressure on MCO, and MCO puts pressure on PBMs); PPLP003544323, Purdue Sales Training presentation; ENDO-CHI_LIT-00078223, co-pay concerns training, Sales Reps are trained to respond with overall economic cost benefits such as fewer additional medications or additional rescue meds. If Step Therapy Trial or

Direct-to-Consumer Marketing

84. In the 1980s pharmaceutical companies discovered the powerful impact that consumers could exert on prescribing decisions when they learn about drugs via media coverage, public relations efforts, news stories, and even advertisements for prescription medications. Marketers learned that DTC marketing and advertising could move a drug quickly through the early stages of the drug life cycle and rapidly increase adoption and expand sales by increasing patient and prescriber awareness of treatment alternatives.[155] However, DTC marketing may also trivialize drug use by making drug consumption a part of everyday life, mislead or confuse consumers, and increase costs by promoting more expensive brand name medications.[156] [157]

85. Currently, branded pharmaceutical manufacturers spend approximately six billion dollars annually marketing medications directly to consumers to increase awareness of drugs and

Prior Authorization is required, the sales reps are instructed to educate the doctor then teach the doctor "how to provide clinical rationale or documentation of a step therapy failure/prior authorization." This includes helping the doctor through the process step-by-step; ACTAVIS0578801, the Willie Sutton rule invoked.

[155] I distinguish between DTC marketing which encompasses all aspects of direct consumer activities from DTC advertising, which as a term of art has come to represent media advertisements for prescription medication that are commonly seen on TV and in magazines.

[156] Shimp T and Dyer R. The Pain-Pill-Pleasure Model and Illicit Drug Consumption. J of Consumer Research, 1979 June;6(1):36-46.

[157] Regarding the pros and cons of DTC marketing, see e.g., Donohue J. A History of Drug Advertising: The Evolving Roles of Consumers and Consumer Protection. The Milbank Quarterly 2006; 84(24):659-699; Perri M and Nelson A. An Exploratory Analysis of Consumer Recognition of Direct to Consumer Advertising of Prescription Medications. J of Heath Care Marketing 1987; 7:9-17; Perri M and Dickson WM. Consumer Reaction to a Direct to Consumer Prescription Drug Advertising Campaign. Journal of Health Care Marketing 1988; 8:66-69; Perri M. The Past, Present and Future of Direct to Consumer Advertising in the Pharmaceutical Industry. Clinical Therapeutics 1999; 21:1798-1811.

stimulate patient requests.[158] [159] [160] Patient requests for a medication have been shown to substantially affect prescribing decisions, even when the requested medications are dangerous, and even when the drug itself was not directly advertised to consumers.[161]

86. The influence of DTC marketing on consumer awareness and actions with respect to opioids that are not advertised to patients through the media is indirect. Patients learn about drugs from other sources such as friends or family who take medications, advocacy groups who seek to increase awareness of diseases or treatments, and internet searches. Advocacy groups, such as the U.S. Pain Foundation, American Academy of Pain Medicine, or the American Pain Society, are an effective way for a pharmaceutical marketer to reach consumers without disclosing their commercial interests.

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[158] https://us.kantar.com/business/health/2017/drug-advertising-booms/ (last accessed February 28, 2019) Jon Swallen, Drug Advertising Booms to $6.4 Billion, May 8, 2017.

[159] Koch-Laking A and Park M. Q/Does DTC advertising affect physician prescribing habits? Journal of Family Practice 2010: 59(11);649-50; Arney J, Street R and Naik A. Factors Shaping Physicians' Willingness to Accommodate Medication Requests. Evaluation & the Health Professions. 2014; 37(3):349-365; Huh J and Langteau R. Presumed Influence of Direct-to-Consumer (DTC) Prescription Drug Advertising on Patients, The Physician's Perspective. Journal of Advertising, 2007; 36(3):151-172; Kravitz R, Epstein R et. Al., Influence of Patients' Requests for Direct-to-Consumer Advertised Antidepressants, A Randomized Controlled Trial. JAMA 2007; 293(16):1995-2002; Mintzes B, Barer ML, Kravitz RL, et al. How does direct-to-consumer advertising (DTCA) affect prescribing? A survey in primary care environments with and without legal DTCA. Canadian Medical Journal (CMAJ) 2003;169(5):405–412. Campbell EG, Pham-Kanter G, Vogeli C, et al. Physician acquiescence to patient demands for brand-name drugs: Results of a national survey of physicians. JAMA. 2013; 173(3):1–3. Becker S and Midoun M. Effects of Direct-to-Consumer Advertising on Patient Prescription Requests and Physician Prescribing: A Systematic Review of Psychiatry-Relevant Studies. J Clin Psychiatry. 2016 October; 77(10):e1293-99; Weissman J, Blumenthal D, Silk A, Newman M, Zaper K, Leitman R and Feibelman S. Physicians Report On Patient Encounters Involving Direct-to-Consumer Advertising. Health Affairs, 2004 (Jan-Jun); Vol Suppl Web Exclusive. W4-219-33; Aiken, K, Swasy J, and Braman A. Patient and Physician Attitudes and Behaviors Associated with DTC Promotion of Prescription Drugs – Summary of FDA Survey Research Results. Final Report, November 19, 2004. https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM600276.pdf (last accessed November 25, 2018).

[160] PPLPC029000182401, IMS, 2006, p.30.

[161] See e.g., McKinlay J, Trachtenberg F, Marceau L, Katz J, and Fischer M. Effects of Patient Medication Requests on Physician Prescribing Behavior: Results of a Factorial Experiment. Med Care. 2014 April; 52(4):294-299. Recognition of this fact is also made by Defendants in documents such as the Opana ER Quarterly Business Review where it is noted, "Targeted patient communications: increase adherence and to increase treatment discussion with HCP," ENDO00125324.

87. Patients see and hear messages from advocacy groups, which increases awareness and stimulates discussion with prescribers in the same fashion as advertisements. Further, advocacy groups are generally perceived to be unbiased and trustworthy, increasing the credibility of this source of drug information. However, there are concerns regarding this route of persuasion because manufacturers' financial support of advocacy groups appears to be linked to *"opioid friendly," "amplified and reinforced messages favoring increased opioid use"* by these groups.[162]

88. DTC marketing also includes targeted patient education, such as, community-based talks designed for patients and caregivers, and other ways (e.g., patient brochures) of reaching patients with marketing messages.[163] These methods are effective for increasing awareness and stimulating patients to have discussions with prescribers. Indirect methods, such as the use of advocacy groups or direct patient contact via brochures and self-help aids, are additional ways for pharmaceutical marketers to reach prescribers vis-a-vis patients with messages about drugs.

Marketing Messages Are Different from the Package Insert

89. While the package insert (PI) is a part of a company's marketing, a drug's marketing is far more comprehensive than the PI and includes all materials, techniques, communications, and messages used to promote the drug.[164] In fact, one goal of drug marketing is to distill and communicate the technical information, or "drug features," in the PI into a few, brief talking

[162] Fueling an Epidemic (Report Two), Exposing the Financial Ties Between Opioid Manufacturers and Third-Party Advocacy Groups. U.S. Senate Homeland Security & Governmental Affairs Committee, Ranking Members Office; https://www.hsdl.org/?abstract&did=808171 (last accessed December 20, 2018); Fueling an Epidemic, Supplement to the February 2018 Report, https://www.hsgac.senate.gov/imo/media/doc/SUPPLEMENT-Fueling%20an%20Epidemic-Exposing%20the%20Financial%20Ties%20Between%20Opioid%20Manufacturers%20and%20Third%20Party%20Advocacy%20Groups.pdf (last accessed December 20, 2018). Rothman S, Raveis V, Friedman B and Rothman D. Health Advocacy Organizations and the Pharmaceutical Industry. Am J of Public Health. 2011; 101(4):602-609.

[163] See e.g., END00717275 p.25; TEVA_MDL_A_11575927 (Fentora, patient as customer).

[164] The PI establishes the boundaries for what information or messages a pharmaceutical company, or other supply chain stakeholder, can discuss in its marketing.

points, which marketers seek to communicate as "drug benefits."[165] [166] This means marketers can be selective in what they choose to talk about in a sales encounter, but the information selected must be consistent with the PI. For example, a sales encounter might include statements about drug benefits that are designed to reduce concerns about the medication and stimulate prescribing but might not include information about potential harms.[167] [168] [169]

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[165] Drug features are the notable characteristics of the drug. For example, features might include a once a day dosage form, a smaller tablet size, or improved efficacy. Marketers seek to turn drug features such as these into customer benefits, in this example, better medication adherence, an easier to swallow table, or better pain relief respectively.

[166] In a sales situation, product benefits, or the "talking points" used by a PSR are limited by the amount of time available to communicate with a prescriber. For most prescribers this will be only a few minutes, placing time pressure on the sales encounter, and limiting the information that can be presented or discussed. See e.g., Wickline_MNK Deposition, pp.33-34; Gordon D. November 15, 2002, Dealing With Drug Reps. Physicians Practice e-newsletter. http://www.physicianspractice.com/operations/dealing-drug-reps (last accessed November 16, 2018); Matthew Arnold, Shadowing The Reps. Medical Marketing and Media Online, November 2012;39-42. https://biopharmaalliance.com/uploads/Shadowing_the_reps_MM_M.pdf (last accessed November 16, 2018).

[167] See e.g., "Proactively neutralize opioid abuse issues." (ENDO00001522, 2002 EN3203 Marketing Plan). This is an example of how they downplayed objections. In this same plan, Endo recognized that oncologists are not afraid of abuse issues with cancer patients, further suggesting they knew abuse was a big issue with doctors, but, they still strategized to neutralize this objection to their product. See also, citation on handling objections.

[168] Mintzes B, Lexchin J, Sutherland J, Beaulieu M, Wilkes M, Durrieu G, and Reynolds E. Pharmaceutical Sales Representatives and Patient Safety: A Comparative Prospective Study of Information Quality in Canada, France and the United States. J Gen Intern Med 28(10):1368-75; Melnick A. Package Inserts – Confusion or Clarity? AMWA Journal 23(3):121-124; Matheson, A. Marketing trials, marketing tricks – how to spot them and how to stop them. Trials (2017) 18:105.

[169] Handling objections and reducing concerns prescribers may have about a medication is a staple of sales training and development. See e.g., Common Objections and Appropriate Responses, JAN-MS-03007298 which was circulated to Nucynta PSRs in May of 2010 (parent email is JAN-MS-007291). This document is a script for PSR conversations with prescribers, and it has messages including, head-to-head comparisons between Nucynta and Tramadol, and Nucynta's superior GI tolerability to Oxycodone, based on the "10-day End Stage Joint Disease" trial data (The FDA deemed the comparisons (head-to-head) and the data on which it is based as misleading (JAN-0003-0002930, FDA Letter to Janssen); Kadian Objection Handler, ACTAVIS0003698; 0a8_ACTAVIS0829193; Objection Handling Workshop, ENDO-OPIOID_MDL-02489844; Taking Aim at Objections, Combunox, ALLERGAN_MDL_03502668; ENDOSell™ Objection Handling, ENDO00023594 in Opana ER Competitor Knowledge Product and Therapeutic Learning System (Sales Training and Development, April 2009) ENDO00023515; Revopan™ Workshop, December 9, 2010, ENDO-CHCI-LIT-00053081; Delivering the Difference, ENDO-CHI_LIT-00166509; Field Coaching Report, Kristiana Wright DSM, INSYS-MDL-007215874; BRM Training, INSYS-MDL-008344022; (Sales) Training Progress Report, JAN00068321; Xartemis XR BroadcastScript March 17, 2014, MNK-T1_0000702315;

90. However, the PI is different than these carefully crafted promotional messages focused on turning drug features into benefits. The PI is technical and scientific information. It is not intended to be promotional.[170] Because time is limited in the sales encounter, and because drug benefits rather than technical descriptions of drug features are what persuade a prescriber, marketers do not use the PI as their primary tool, even though it must generally be referenced.[171] Marketing messages (i.e., the information-flow that turns a drug feature into a drug benefit) are created with information the marketer wants the Customer to see and hear, not just a summary of the PI.

91. Pharmaceutical marketers, including Defendants, use many channels to communicate their messages or "talking points" to prescribers, including: personal selling (detailing), use of medical literature, continuing medical education (CME), development of clinical guidelines, sponsored meals, and opportunities for interactions with other prescribers (opinion leadership, peer-

Delta Point, Inc. Proposal for Pennsaid and Exalgo, MKNK-T1_000094043; September 25, 2000 Memo, November 13, 2000 Phase II Training Program, E16_00002947; Workshop 6: REV it Up! Nucynta National Meeting, JAN00047720; Managers Meeting 2007, Sales Training, TEVA_MDL_A_00358559 (focus on managed care); Fentora Training, TEVA_MDL_A_00359511.

[170] While the PI is intended to be non-promotional, this was not always the case. The development of the OxyContin PI was described as: *"The evolution of the package insert from its original draft over four years ago was a particularly interesting and informative process. Dr. Curtis Wright, the FDA medical reviewer, upon first reviewing it, stated that he had never seen a package insert with as much promotional and marketing material in it as ours. (Clearly our package insert team, representing Medical, Scientific Communications, Pharmacokinetics and Drug Metabolism, and Marketing, did its job skillfully.) Dr. Wright even told us that all of this promotional material would disappear. It did not. In fact, the package insert contains all of the major elements of our long-range marketing platform for this drug and proved most valuable when it came time to negotiate promotional copy with the Division of Drug Marketing, Advertising and Compliance, DDMAC. We argued extensively with DDMAC in January through March of this year. The result of these, "discussions" was a tremendous set of promotional claim rich copy. And the consequence? About 50 million in sales in the first year, more than 37,000 prescriptions per month, and a market share approaching 13 percent. That is quite a beginning."* (RS030719 Sackler, Richard, pp.202-203 and Exhibit 30).

[171] PDD1502332817, Purdue Key Selling Points memo and Pri-Med meeting information.

influence).[172] [173] [174] [175] The use of sales representatives is the primary way pharmaceutical manufacturers educate prescribers and shape prescribing behavior.[176] [177]

[172] See e.g., Adair RF and Holmgren LR. Do drug samples influence resident prescribing behavior? A randomized trial. Am J of Medicine 2005; 118(8):881-884; Avorn J, Chen M, and Hartley R. Scientific Versus Commercial Sources of Influence on the Prescribing Behavior of Physicians. Am J of Medicine 1982; 73:1-7.

[173] See e.g., Spiller L, and Wymer W. Physicians' Perception and Uses of Commercial Drug Information Sources: An Examination of Pharmaceutical Marketing to Physicians. Health Marketing Quarterly, Vol. 19(1) 91-106; Ndosi M, and Newell R. Medicine information sources used by nurses at the point of care. Journal of Clinical Nursing, 19, 2695-2661; McGettigan P, Golden J, Fryer R and Feely J. Prescribers prefer people: The sources of information used by doctors for prescribing suggest that the medium is more important than the message. J of Clin Pharmacol, 51, 184-189; Pines A. Patient information leaflets: friend or foe? Climacteric 2015; 18:664-665.

[174] See e.g., 2007 FSMB Fishman sponsor Responsible Opioid Prescribing, PPLP003477086; 2011 December Webster study PPLP003278561; 2007 Clinical Journal of Pain Article Challenges in Development of Rx Opioid Abuse-deterrent Formulations, JAN0015797; 2003 Duragesic Key Tactics Review, JAN-MS-00306778; 2009 Tapentadol Unbranded Acute Pain Message Platform, JAN-MS-00339425; Primary Care Medical Education Plans 2007, JAN-MS-00410975; Tapentadol Publication Client Status Report, JAN-MS-00437356; EN3203 Marketing Plan, ENDO00001522; Opana Business Plan 2005, ENDO0000923; MoxDuo Launch Playbook, ACTAVIS0320237 (publication plans).

[175] See e.g., Lubloy A. Factors affecting the uptake of new medicines a systematic literature review. Health Services Research 2014; 14:469-94; Fugh-Berman A, Alladin K and Chow J. Advertising in Medical Journal: Should Current Practices Change? PLoS Medicine, 2006; 3(6):e130, https://journals.plos.org/plosmedicine/article/file?id=10.1371/journal.pmed.0030130&type=printable (last accessed December 9, 2018).

[176] Direct sales through pharmaceutical representatives is the single largest marketing expense for most pharmaceutical companies. See e.g., Share of promotional spending of top 20 pharmaceutical companies in the U.S. by allocation in 2013. (68%) https://www.statista.com/statistics/388002/promotional-spending-allocation-from-top-20-pharma-companies-in-the-us/ (last accessed November 7, 2018); Pharma Promotional Spending in 2013: Professional eDetailing, DTC Advertising, Professional Meetings, Journal Advertising. Pharma Guy, http://www.pharma-mkting.com/articles/pmn1305-article01/ (last accessed, March 9, 2019).

[177] See e.g., Spurling G, Mansfield PR, Montgomery BD, Lexchin J, Doust J, Othman N, Vitry AI. Information from Pharmaceutical Companies and the Quality, Quantity and Cost of Physicians' Prescribing: A Systematic Review. PLoS Med 2010. 7(10):e1000352; Brody, H. The Company We Keep: Why Physicians Should Refuse to See Pharmaceutical Representatives, (Reflection). Annals of Family Medicine 2005; 3(1):82-85. Findings include: higher prescribing, higher cost of drugs and less appropriate (quality) prescribing.

92. Prescribers are exposed to marketers' carefully-crafted information[178] which is designed to be and is effective in generating prescription sales.[179] This implies prescribers see and hear information that marketers want them to see and hear, including information that goes beyond the scope of the package insert. Specifically, pharmaceutical companies provide information intended to induce the writing of prescriptions. Marketing principles suggest, and my experience confirms, prescribers consider all the information, from all sources, that is communicated to them by pharmaceutical companies, and rarely rely on the PI alone.[180]

[178] While product labeling must conform to FDA requirements, when a sales representative discusses a drug with a prescriber, the sales representatives decides what information is covered and where emphasis is placed.

[179] See e.g., Wood SF, Podrasky J, McMonagle MA, Raveendran J, Bysshe T, Hogenmiller A, et al. (2017) Influence of pharmaceutical marketing on Medicare prescriptions in the District of Columbia. PLoS ONE 12(10): e0186060.; Brax H, Fadlallah R, Al-Khaled L, Kahale LA, Nas H, El-Jardali F, et al. (2017) Association between physicians' interaction with pharmaceutical companies and their clinical practices: A systematic review and meta-analysis. PLoS ONE 12(4): e0175493.; Spurling G, Mansfield PR, Montgomery BD, Lexchin J, Doust J, Othman N, Vitry AI. Information from Pharmaceutical Companies and the Quality, Quantity and Cost of Physicians' Prescribing: A Systematic Review. PLoS Med 2010. 7(10):e1000352; Steinman MA, Bero LA, Chren MM, Landefeld CS. Narrative Review: The Promotion of Gabapentin: An Analysis of Internal Industry Documents. Ann Intern Med. 2006; 145:284-293; Ahmed, R.R., Vveinhardt, J., Streimikiene, D., and Awais, M., 2016. Mediating and Marketing Factors Influence the Prescription Behavior of Physicians: An Empirical Investigation. Amfiteatru Economic, 18(41), pp. 153-167; Katz D, Caplan A, Merz JF. All Gifts Large and Small: Toward and Understanding of the Ethics of Pharmaceutical Industry Gift-Giving. Am J Bioethics 2010; 10(10):11-17; Gonul, F., Carter, F., Petrova, E., & Srinivasan, K. (2001). Promotion of prescription drugs and its impact on physicians' choice behavior. Journal of Marketing, 65, 79–90; DeJong C, Aguilar T, Tseng CW, Lin G, Boscardin W, and Dudley A. Pharmaceutical Industry-Sponsored Meals and Physician Prescribing Patterns for Medicare Beneficiaries. JAMA Internal Medicine. 2016; 176(8):1114-1122; King M and Bearman PS. Gifts and influence: Conflict of interest policies and prescribing of psychotropic medications in the United States. Social Science and Medicine 2017; 172:153-162.

[180] See e.g., Wickline_MNK Deposition p.33; Bingol, Demir_Endo Deposition, pp.199-200 and Endo-Bingol-Exhibt 16.

Branded and Unbranded Marketing

93. In pharmaceutical marketing, branded marketing is the promotion of a specific drug, by the drug's name and its indication. The FDA regulates branded marketing.[181] Manufacturers submit advertising materials to the FDA's Office of Prescription Drug Promotion (OPDP), but FDA approval prior to dissemination is not required. Thus, inaccurate or unbalanced advertisement may be in circulation until the FDA identifies them.[182] The FDA can intervene by way of a warning letter for advertising materials that it finds do not accurately convey a drug's labeling. FDA's oversight of advertising can be delayed, allowing improper advertising materials to reach a large audience before being pulled back.[183]

94. Pharmaceutical marketing is also done through unbranded channels. Unbranded marketing includes activities that create awareness of a disease or condition, advocate for patient care or prepare a favorable environment in the marketplace for sales, without mentioning a drug's name and indication together. While unbranded advertisements often target patients; health professionals are exposed to these advertisements in the media as well. Unbranded advertisements focus on symptoms and encourage viewers to talk to their doctor about

[181] All advertisements and promotional labeling for an FDA approved medication are required to be submitted when they are first used or disseminated on a form FDA-2253. https://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/AdvertisingLabelingPromotionalMaterials/ucm118171.htm; Instructions for Completing Form 2253, https://www.fda.gov/downloads/aboutfda/reportsmanualsforms/forms/ucm375154.pdf, (last accessed August 1, 2018). Though this does not mean that all advertisements and promotional labeling are reviewed by the FDA.

[182] It is my understanding that the OPDP is substantially understaffed in its ability to review the tens of thousands of pieces of advertising materials that come across its desk each year. The OPDP has fewer than 75 people on staff to review the approximately 75,000 pieces of advertising material it receives each year.

[183] A Government Accountability Office report from 2008 detailed that it takes the FDA about 7 months to organize a warning letter and another 4 months on average for manufacturers to respond to it by removing or adjusting their advertising materials. https://www.gao.gov/new.items/d08835.pdf (last accessed February 28, 2019).

treatment.[184] Unbranded advertisements get patients thinking and talking about their disease with the goal of seeking treatment, which might include a prescription medication.[185] [186]

95. Marketers disseminate unbranded marketing messages directly, but a subtler form of unbranded advertising is when pharmaceutical marketers work with external organizations, such as the advocacy groups discussed above, with an interest in a specific disease, condition or even symptoms. Part of the appeal of unbranded advertising is that this form of advertising is generally perceived as neutral, "grassroots," unbiased or scientific, but this can be misleading for two reasons. First, unbranded advertising does not have to inform the patient of the risks of a medication, conferring greater safety of use. Second, the advertising may be disseminated through a third-party organization that is funded by the marketer creating concerns for commercial bias in the information disseminated.[187]

[184] See e.g., 2001 OxyContin Budget Plan, SHC-000001165, p.32-34; ENDO-CHI-LIT-00113093, p.6.

[185] See e.g., Alves T, Mantel-Teeuwisse A, Paschke A, Leufkens H, Puil L, Poplavska E, and Mintzes B. Unbranded advertising of prescription medicines to the public by pharmaceutical companies. Cochrane Database of Systematic Reviews, 2017, Issue 7. Art. No. CD012699. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012699/epdf/full (last accessed December 27, 2018); Beth Snyder Bulik, Unbranded pharma ads - what are they good for? Actually quite a bit, marketing panelists say. FiercePharma, March 11, 2018. https://www.fiercepharma.com/marketing/unbranded-pharma-ad-what-are-they-good-for-actually-quite-a-bit-marketer-panelists-say (last accessed December 27, 2018); Aimee Picchi, The rise of the "unbranded" pharmaceutical ad. CBS News, MoneyWatch, August 30, 2016. https://www.cbsnews.com/news/the-rise-of-the-unbranded-pharmaceutical-ad/ (last accessed December 27, 2018).

[186] Rollins B, King K, Zinkhan G, and Perri M. Nonbranded or Branded Direct-to-consumer Prescription Drug Advertising – Which is More Effective? Health Marketing Quarterly, 2011; 28(1):86-98.

[187]Fueling an Epidemic (Report Two), Exposing the Financial Ties Between Opioid Manufacturers and Third-Party Advocacy Groups. U.S. Senate Homeland Security & Governmental Affairs Committee, Ranking Members Office; https://www.hsdl.org/?abstract&did=808171 (last accessed December 20, 2018); Fueling an Epidemic, Supplement to the February 2018 Report, https://www.hsgac.senate.gov/imo/media/doc/SUPPLEMENT-Fueling%20an%20Epidemic-Exposing%20the%20Financial%20Ties%20Between%20Opioid%20Manufacturers%20and%20Third%20Party%20Advocacy%20Groups.pdf (last accessed December 20, 2018). Rothman S, Raveis V, Friedman B and Rothman D. Health Advocacy Organizations and the Pharmaceutical Industry. Am J of Public Health. 2011; 101(4):602-609.

96. Defendants utilized unbranded marketing,[188] including partnering with advocacy organizations such as the American Pain Foundation, American Pain Society, American Academy of Pain Medicine, and many other regional and national organizations, to deliver unbranded marketing messages related to the use of opioids.[189]

97. While unbranded marketing is perceived in a generally positive way by patients and may not be scrutinized by regulatory agencies in the same manner as branded marketing, unbranded marketing by companies should follow the same pharmaceutical marketing standards identified above.

II. MARKETING IN THE PHARMACEUTICAL SUPPLY CHAIN

98. Pharmaceutical marketing is implemented through an integrated supply chain (Figure 4). The stakeholders in this system work together to market, sell, and pay for pharmaceutical products. The U.S. pharmaceutical supply chain is composed of manufacturers, wholesale distributors, and pharmacies in the distribution of medicines and other stakeholders that coordinate revenue

[188] See e.g., JAN-MS-00339425 tapentadol unbranded message platform, p.2.

[189] Documents related to planning and execution of work with advocacy groups can be seen in, e.g., ENDO-OPIOID-01606654, email and attachments detailing Endo support of International Neuropathic Pain Conference; Advocacy, Policy, Quality Activities, JAN00038605; JAN-MS-00000205; JAN-MS-00132620; JAN-MS-00264703; JAN-MS-02508517; JAN-MS-00932379; JAN-MS-00922821; JAN-MS-006322008; (Purdue) Treatment Options: A Guide for People Living with Pain, 2007 American Pain Foundation; Purdue Grants and Giving, PPLP0033465134; 2012 Actavis MoxDuo Staffing Plan/SOW, The Cutting Edge of Pain Program (Partner with American Pain Society) ACTAVIS0316645; ENDO-CHI_LIT-00012357, Opana ER Tactical Plan Meeting 7/1/2010, public service ads about "bad" programs, p.4; ENDO-CHI_LIT-00098421, p.14, 21-24, 45; Draft Document, 2011 Oxymphone Franchise Tactical Plan Review, Demir Bingol, Sr. Product Director, ENDO-CHI_LIT-00546731 pp.80-88; ACTAVIS0771831 (APS Website); ENDO-CHI_LIT00543506, OxyM Issues Management: Overall Approach, Stakeholder Communications and Crisis Management Strategies, May 10, 2006; Subsys Launch Playbook, "Non-Sales Force Communication to Core Targets," INSYS-MDL-000458120, p.21-23; MNK-T1_0000214460, Government Affairs, Policy and Advocacy, September 14, 2014; Advocacy and the Pain Franchise, October 16, 2013, MNK-T1_0000222031. Deposition testimony also confirms interactions and work with advocacy groups, e.g., Deem-Eshleman_Janssen, p.59-65; Hassler-Teva_30B6, pp.331-332; Moskovitz_Janssen_Vol.1_30(B)(6), pp.228-230 and Exhibit 17; Spokane_Teva, pp.40-41; Wickline_MNK, pp.159-161; Altier-Allergan, pp.125-129; Barrett_Allergan, pp.114-118, 279-281; Koch_Purdue, pp.178-180; Krishnaraj_Insys, pp.197-201; INSYS-MDL-014996303 Masters January 4, 2017 email with subject Donation Letter of Agreement – Final Attached for Signature (Pain Foundation) and the Donation Letter of Agreement, INSYS-MDL-014996304 and Invoice, INSYS-MDL-014996309.

flows. Supply is ensured for prescription opioids by manufacturers, including Purdue, Endo, Janssen, Teva, Cephalon, Allergan, Insys, and Mallinckrodt, and their families of companies. Wholesale distribution of pharmaceuticals in the U.S. is highly concentrated, with AmerisourceBergen, Cardinal Health, and McKesson accounting for about 85% of the total market share of wholesalers.[190] Large pharmacy chains such as CVS, Walgreens, and Walmart also engage in internal wholesale distribution of medicines, acting as their own distributors either alone or in cooperation with wholesale distributors.[191]

99. The goal of the pharmaceutical supply system is to move products from manufacturers to the Customer. Each stakeholder has the common goal of selling pharmaceuticals by working with and through others in the supply chain system. Defendants had agreements to distribute products and marketing messages related to opioids.[192] The primary messages in relation to wholesale distributors are expected to be focused on price, quality, drug availability, and service.[193] However, pharmacists that dispense prescriptions may also receive promotional messages focused on drug features and benefits, similar to prescribers.[194] This is important to

[190] Dabora M, Turaga N, and Schulman K. Financing and Distribution of Pharmaceutical in the United States. JAMA. Published online May 15, 2017. https://jamanetwork.com/journals/jama/fullarticle/2627994 (last accessed December 18, 2018).

[191] CAH_MDL2804_02376356, CVS Agreement (Matt Leonard).

[192] See Schedule 16: Co-Promotional Marketing with Distributor Defendants.

[193] [redacted]

[194] See e.g. the Purdue sponsored counseling guide for pharmacists, PDD1502310593. Sponsored educational letter and pamphlet from Purdue to pharmacies regarding pain and OxyContin. The core promotional messages in this guide are consistent with the messages in Section IV: Defendants Marketing of Opioids, of this Report and include: "there is a difference between 'addiction' and 'pain-relief seeking' behavior." p.4; "It is rare for patients with intractable pain to abuse or divert their prescribed pain medication." p.5; "Two opioids with minimal risk for diversion and abuse include OxyContin and MS Contin." p.5; "Pain is one of the most common reasons people consult a physician, yet it frequently is inadequately treated, leading to enormous social cost in the form of lost productivity." p. 3; "True addictive behaviors rarely occur in patients who utilize opioids for chronic pain, especially when the patient has no prior history of substance abuse." p. 4; "Physical dependence occurs with the continual use of many medications including beta-blockers, antidepressants, corticosteroids, opioids, and others." p. 4; "It is rare for patients with intractable pain to abuse or divert their prescribed pain medication.", p. 5; Effective strategies for cancer pain include: "aggressive use of long-acting, oral opioids as first-line

pharmaceutical companies who will lose sales if resistance to their drug is encountered at any point in the system.

100. Revenue flows (Figure 4) between various parts of the supply chain system in a variety of forms, including payments, rebates, and chargebacks that ensure members of the supply chain system have data, such as utilization, supply, and distribution, showing exactly where each bottle of pills is going and at what price.[195] [196] This data is used in financial planning, manufacturing, and marketing of pharmaceuticals and provides critical metrics to pharmaceutical marketers for assessing past, and planning future, marketing efforts.[197]

101. Given the complexity of revenue flows, wholesalers and manufacturers have a synergistic relationship, each relying on the other to sustain sales. The wholesale function is also important to retail pharmacy, as wholesalers offer attractive pricing in connection with their negotiation of volume discounts with manufacturers. This is especially important for generic medicines, where pharmaceutical wholesalers can give preferential treatment to a specific manufacturer's products by stocking only (or preferentially) selected manufacturer's products for distribution and, or generic purchasing programs.[198]

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therapy . . . and encouraging the use of short-acting opioids to provide for relief of 'breakthrough' pain." p. 7; "Medications for persistent cancer-related pain should be administered on an around-the-clock basis." "Opioid tolerance and physical dependence are expected with long-term opioid treatment and should not be confused with addiction." p. 7; "[A]gents that do not have a 'ceiling effect' to their analgesic efficacy and will not reverse or antagonize the effects of other opioids administered at the same time are called 'full agonists.'" p. 7; "[T]he overall risk of inducing addiction with opioid agonists in patients with intractable pain is rare." p. 8.

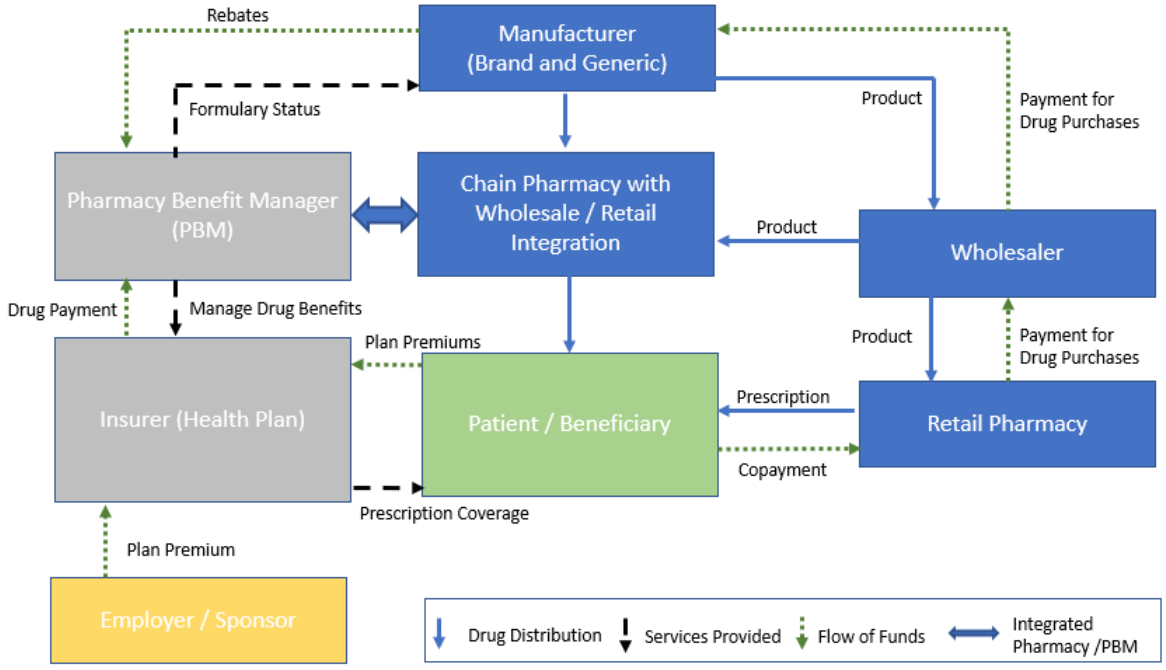
[195] Manufacturers routinely negotiate contract prices with customers such as retail pharmacy operations. Wholesalers ensure that each customer ultimately pays their contracted amount through a system of contracts, chargebacks, and rebates. See Figure 4: Flow of Services, Product and Funds in the Pharmaceutical Supply Chain System.

[196] See e.g., 2010 Cardinal Health Presentation, CAH_MDL2804_02103500; Seid email chain with subject, HDMA Marketing Conference Follow Up, PPLPC008000041397.

[197] See e.g., JAN-MS-01117436, Trade Analytics – Managed Markets Summit, October 18, 2012, trade analytics managed sales and marketing data with distributors; JAN-MS-00454956, 2012 email chain with subject High Level Overview of JOM CII and SOM Process.doc, tracking of inventory.

[198] Wholesalers seek to be a "one-stop" provider of generics for pharmacies of all types. McKesson offers two general programs called the OneStop Generics™ and SynerGx®generic drug purchasing and distribution programs. These programs offer customers cost savings and product availability, avoiding

Figure 4: Flow of Services, Product, and Funds in the Pharmaceutical Supply Chain System[199]



shortages and out-of-stock situations in exchange for McKesson selecting the generic manufacturers that will be the primary sources of generic products. This gives McKesson the ability to move market share. https://www.mckesson.com/pharmaceutical-distribution/generic-drugs/ (last accessed December 13, 2018). See e.g., [redacted]

[199] This figure represents the flow of funds for brand name drugs purchased in retail pharmacies managed by pharmacy benefit managers for an employer sponsored health plan. The figure is adapted from "Prescription Drug Pricing in the Private Sector," January 2007. The Congress of the United States, Congressional Budget Office.

Table 1: Pharmaceutical Supply Chain System Stakeholders

Entity	Supply Chain System Roles
Pharmaceutical Manufacturers - Branded - Generic - Specialty	• Drug development, manufacturing, and marketing • Set prices • Negotiate discounts, rebates • Clinical trial research and drug supply
Wholesale Distributors - Full Service Wholesalers - Warehousing Pharmacy Chains	• Manage distribution of products • Facilitate customer discounts and chargebacks • Service pharmacies / generic source programs • Negotiate pricing with pharmacies
Pharmacies - Retail (Chain and Independent) - Big Box Retail / Food Stores - Mail Order / Specialty / Specialty Pharmacy - Hospitals / Physicians	• Negotiate pricing, discounts, and rebates with manufacturers • Negotiate pricing with wholesale distributors • Contract with pharmacy benefit managers • Dispense and monitor patient outcomes • Sell prescription medication
Insurers, Third-Party Payers Pharmacy and Pharmacy Benefit Managers	• Management of prescription costs for insurers • Formulary Management • Rebate negotiation • Pharmacy network agreements • Mail order • Claims processing
Other stakeholders: Physicians, Employers, Consumers, Caregivers	• Prescribe • Select of PBMs, insurers, pharmacy providers • Monitor patient outcomes

III. DEFENDANTS' MARKETING OF OPIOIDS

A. Background and Competitive Market for Opioids

102. According to the Kadian Learning System,[200] an Allergan sales training manual, the need to regulate controlled substances (which includes opioids) to prevent diversion and abuse (corollaries of addiction) has been on the legislative agenda since about the 1930s. Yet, opioid use has grown over time in response to both patients' need for analgesia and the marketing of drugs to fill that need.[201]

103. Morphine and meperidine have been available as commercial pharmaceutical drugs for many years. With health care professionals, the stigma of morphine limited its use primarily to end-of-life care and cancer pain. In the 1970's the pharmaceutical industry began to market codeine, hydrocodone, and oxycodone products in combination with aspirin or acetaminophen, under trade names such as Tylenol with Codeine (including multiple strengths of the codeine component) Vicodin and Percocet.[202] Over time, utilization of these drugs grew, but health professionals remained conservative in their prescription of opioids.[203]

104. In about 1982, Lortab (hydrocodone and acetaminophen) was approved for treating "mild to moderate" chronic pain. Five years later, Purdue's MS Contin (extended release morphine sulfate), which at the time did not have approval from the FDA as a new drug, was marketed as a "generic" morphine product prior to its formal approval under a new drug application by the FDA. Because of problems with orally administered morphine, Purdue was eager to introduce its MS Contin because of its new, extended-release formulation.[204]

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[200] Kadian Learning System, Chapter Six: Drug Abuse and Chronic Pain, ALLERGAN_MDL_00436784, p.00436786.

[201] Other sales training manuals and scripts are identified in Schedule 11.

[202] Percodan was an oxycodone/aspirin combination.

[203] Richard Sackler, M.D., August 28, 2015, Deposition in Civil Action No. 07-CI-01303, p.18.

[204] The "Contin" delivery system uses a polymer matrix to create sustained delivery of the embedded drug. This system uses a water based and a non-water (hydrophobic) based polymer, blending the drug with the water-based polymer. When combined, the drug dissolves from the water-based component

105. In 1991, a unique product, Duragesic (fentanyl transdermal patch), was introduced to provide long-acting delivery of fentanyl for patients who needed sustained analgesia. Duragesic was direct competition for MS Contin in the extended release category of analgesia. Other competitors included hydromorphone and oxycodone combinations, but these did not provide for extended release.

106. During these early years up to about 1994, according to Purdue market research, the Class II opioid market was growing at a rate in excess of 12 percent each year. However, oxycodone combination product sales had slowed, and according to Purdue, this was likely due to the introduction of long-acting opioid formulations which were capturing market share, and that Class III opioids (e.g., hydrocodone) were easier to prescribe. Interestingly, Purdue also noted clinical equivalence between the oxycodone products and hydrocodone products in the OxyContin launch plan: *"Although no therapeutic difference has been demonstrated, Class III opioids are easier to prescribe because they can be phoned into the pharmacy and do not require a triplicate prescription."*[205] Further, marketing planners at Purdue realized its MS Contin would soon be subject to generic competition and worked to develop a strategy to replace its vulnerable MS Contin sales with sales of its newer, long-acting oxycodone product, OxyContin.[206]

107. By 1995, Purdue had developed extensive marketing plans for the launch of OxyContin.[207] This planning was effective as Purdue's OxyContin sales increased to nearly $1 billion in 2000 and estimated sales in excess of $1.3 billion in 2001.[208] During about the same time period, Purdue's sales force grew from 256 PSRs in 1995 to 674 PSRs in 2000.[209] The rapid increase in the market

limited by the rate of the hydrophobic component. This delivery matrix provides the original drug at a slower rate over a longer period but does not alter the active ingredient.

[205] OxyContin™ Launch Plan, September 27, 1995. PDD1501011301.

[206] Id.

[207] 1995 OxyContin Launch Plan, PURCHI-003286149, pp.1-5.

[208] 2002 Budget Plan, OxyContin, SHC-000001228, p.7.

[209] OxyContin Market Events, PPLP012000371063.

for pain control attracted the attention of other manufacturers, and the market expanded with the addition of other branded opioid products such as Kadian (morphine sulfate extended-release, Allergan, 1996), Actiq (fentanyl oral lozenge, Anesta, 1998), and Avinza (morphine sulfate, Elan, 2002).

108. Between 1999 and 2003, Endo launched variant strengths of Percocet (a combination oxycodone/APAP product), doubling the maximum strength from 5 mg of oxycodone to 10 mg to capture more of the oxycodone market.[210] In 2006, Endo launched Opana / Opana ER (oxymorphone) with an understanding of the *"hostile,"* regulatory and political environment surrounding new long-acting opioids.[211] Endo's marketing plans for Opana considered the premise that there was little differentiation between Opana and other long acting opioids, but the company wanted to leverage its efficacy and safety data to position Opana as the most complete opioid on the market. Endo utilized messages (discussed in detail below) such as *"Stay ahead of the Pain."*[212]

109. In 2007, Endo introduced Patient Profiles, a teaching tool for sales representatives to help doctors identify patients for treatment with Opana. Endo created fictitious patients, like a carpenter suffering from chronic low back pain, an osteoarthritis patient with knee problems, or a cancer patient, to help sales representatives coach doctors into identifying potential patients in their practice. Each patient profile reflected different Opana features that Endo highlighted as dosing advantages.[213]

110. After the initial boom in the development of long-acting formulations of opioids, some manufacturers focused on reformulating existing drugs. In 2009, Alpharma launched Embeda

[210] ENDO-OPIOID_MDL-04908522; ENDO-OPIOID_MDL-03388210; ENDO-OPIOID_MDL-04136658; ENDO-OPIOID_MDL-04908071.

[211] 2006 Opana Business Plan 1, ENDO-CHI_LIT-00552969; Other Defendants also considered the market environment as unfavorable, with recognized barriers to opioid sales growth, e.g., JAN-MS_00442778, Pain Policy Overview.

[212] END00038091, "Help Your Patients Stay Ahead of Pain."

[213] END00018819, New Sales Tools: Patient Profiles, Bill, Anne, Mike.

which was a combination of morphine and naltrexone. Covidien recognized this trend as well, as noted in their strategic vision, *"Teaching old drugs new tricks to create value,"* and launched Exalgo (long-acting hydromorphone) in 2010.[214]

111. As time passed, the use of opioid analgesics for both medical and non-medical uses grew in the U.S.[215] Alturi (2014) estimated overall opioid use increased by 1,448% from 1996 to 2011, with most of this growth occurring between 1996 and 2004. Misuse increased at three times this rate (4,680% from 1996 to 2011). Further, the increase of opioids for medical uses appears to contribute to increased non-medical use (diversion and abuse).[216]

112. With both medical use and abuse of opioids on the rise, FDA scrutiny of opioid promotional messages resulted in several warning letters being issued to opioid marketers. Cited earlier in this Report, the FDA's letters focused on concerns that promotional materials used by drug makers contained false or misleading statements related to safety and efficacy (i.e., claims opioids were safer and more effective than the scientific evidence would support) and the promotion of opioids beyond their approved indications.

[214] Coviden: Positive Results for Life 2011-2015 Strategic Plan, May 28, 2010, MNK-T1_0000468961.

[215] See e.g., Guy G, Zhang K, Bohm M, Losby J, Lewis B, Young R, Murphy L, and Dowell D. Vital Signs: Changes in Opioid Prescribing in the United States, 2006-2015. US Department of Health and Human Services/Centers for Disease Control and Prevention, Morbidity and Mortality Weekly Report, 2017; 66(26):697-704; Mosher, H, Krebs E, Carrel M, Kabloi P, Vander Weg M, and Lund B. Trends in Prevalent and Incident Opioid Receipt: an Observational Study in Veterans Health Administration 2004-2012. J of General Internal Medicine 2014; 30(5):597-604; Atluri S, Sudarshan G, and Manchikanti L. Assessment of the Trends in Medical Use and Misuse of Opioid Analgesics from 2004 to 2011. Pain Physician, 2014; 17:E119-E128.

[216] Atluri S, Sudarshan G, and Manchikanti L. Assessment of the Trends in Medical Use and Misuse of Opioid Analgesics from 2004 to 2011. Pain Physician, 2014;17:E119-E128.

113. With respect to addiction, Defendants continued to seek ways to expand sales.[217] This included reformulations of existing drugs and focusing on claims of abuse deterrent formulations.[218] [219] To examine ways to reduce abuse, addiction, and deaths from opioids, Purdue's David Haddox, with other researchers, investigated strategies to mitigate the negative health consequences of opioid use.[220] This work modeled three interventions (the introduction of tamper-resistant opioid formulations, marketing aimed at increased prescriber education, and reduced levels of patient abuse) that could impact both opioid sales and potential harm to patients. According to Dr. Haddox, the results of the simulations were based on the best data available, but data he stated was not perfect. From the simulations, the researchers concluded that creating tamper-resistant (abuse deterrent) formulations would increase prescriptions (increasing the total numbers of patients receiving opioids) and reduce the rate of harms (abuse, addiction and death). However, this result meant that the total number of patients who would abuse, become addicted or die from opioid use would increase. Conversely, increased prescriber education was expected to decrease the number of patients addicted, abusing or dying by 50% due to a reduction in the overall use of opioids. In other words, prescriber education about opioid risks was expected to deter prescription writing for opioids. Intervention three, a simulation of reduced patient abuse, also reduced death rates, but to a lesser extent than prescriber education.[221]

[217] See e.g., 2012 10 Year Plan, PPLP004149692; PPLPC016000255303, BDC meeting – Project Tango.

[218] See regarding formulations, e.g., MNK-T1_0000468961 esp. pp.12,18-20, 38; TEVA_CHI_00042923 p.41-42; 2015 Coplan email chain discussing abuse deterrence, or lack thereof, for OxyContin's new formulation, PPLPC019001155586.

[219] New formulations also had value to Defendants in terms of the product lifecycle and patent protection. New formulations may provide additional years of patent exclusivity for products at the end of the patent life, a practice in marketing known as evergreening.

[220] Wakeland W, Schmidt T, Gilson A, Haddox J and Webster L. System Dynamics Modeling as a Potentially Useful Tool in Analyzing Mitigation Strategies to Reduce Overdose Deaths Associated with Pharmaceutical Opioid Treatment of Chronic Pain. Pain Medicine 2011;12:S49-S58.

[221] Haddox Deposition pp.320 -340 and Exhibits 26 and 27.

114. Defendants could infer from these simulations that creating tamper-resistant drugs was the only viable strategy that could possibly lower the rate of abuse while allowing for increasing prescription sales. Executing marketing strategies aimed at education about abuse and addiction, changing perceptions about opioids, would hinder sales. According to Dr. Haddox, Purdue did not use the information developed from these simulations "in any tangible way." He contended that opioid prescriptions in general had begun to decline, and while not making any claim of causality with respect to prescriber education, he believed the company's PSRs emphasized new risk information as it became available.[222]

115. In my opinion, Dr. Haddox's belief that opioid sales were declining was likely due to his awareness of decreasing OxyContin sales, which by this time were impacted by generic and other competition. Through all of this, Purdue's marketing goals did not change. The company's goal was to maximize sales of their opioid drugs, and as the simulation suggested, marketing aimed at increasing prescriber education about abuse and addiction would only serve to further reduce prescriptions. Instead, a focus on tamper-resistance could continue to increase prescriptions. From a marketing perspective, this provided at least two reasons for Defendants' focus on tamper-resistant formulations designed to deter abuse. First, this was a marketing option that would not decrease opioid sales. Second, the tamper-resistant, abuse deterrent message would give physicians a sense of security that they could safely prescribe opioids for their patients which was consistent with Defendants' marketing themes (discussed below).

B. Defendants Sought to Identify Customer Needs

116. A key principle of marketing is to identify an unmet need and work to fill that need. As noted by Dr. Richard Sackler, former President and Chairman of Purdue, the use of opioids to treat pain caused physicians concern because of efficacy, side effects, addiction, and abuse potential.[223]

[222] Id.

[223] Richard Sackler MD, August 28, 2015 Deposition, in Commonwealth of KY, ex rel. v Purdue Pharma L.P., et al. p.18.

Understanding these Customer concerns was important to opioid marketers because it would enable them to better meet Customers' needs.[224]

117. To gain such insights, Defendants analyzed the market for pain medications and conducted marketing research. This market research, dating back to before the launch of OxyContin, included information about physicians and payers concerns (barriers to prescribing) about the safety and risks of opioids.[225] However, research also identified unmet needs, such as physicians' desires for pain medications that lasted longer, had less breakthrough pain, and were not as likely to be abused or diverted. [226] Marketing theory suggests that *if* products existed that could satisfy these Customer needs, prescribing habits should change because these would be significant therapeutic advances in pain treatment. While the pharmacology of opioids did not substantially change, the marketing of opioids did.[227]

118. At Endo, market research told it that one of the "most important strengths" of Opana ER was the perception among HCPs that Opana ER had "low abuse potential."[228] Endo viewed this as "an opportunity" on which it could build.[229] Endo's message was being heard, because over

[224] See e.g., JAN-MS-00306327, Duragesic Evolution Overview, 2003; ENDO-CHI_LIT-00387331, Opana ER Key Business Question and Opportunity Assessment and Insights; Deem_Eshleman_Janssen Deposition, pp.24-28 (market research for the Nucynta brand).

[225] Some of the barriers are discussed in the materials in this Report related to "handling objections."

[226] Purdue focus groups; Xartemis XR User & Non-User Qualitative research Summary Report, MNK-T1_0000136719; Sanjeev August 10, 2013 email with subject: MNK 795 Value Proposition development research findings. MNK-T1_0000180846; Acute Pain Management MNK-795 Value Proposition Qualitative Research, MNK-T1_0000258075; Xartemis XR and MNK 155 Situation Analysis, June 25th, 2014, MNK-T1_0000110204; JAN-MS-00436020 esp. p.17-20, 32-34, 37, etc.; Nucynta ER Payer and Physician Research, JAN-MS-00473858; Opana ER National Advisory Board, ENDO-CHI_LIT-00190053.

[227] See e.g., U.S. Department of Justice, Statement of United States Attorney John Brownlee on the Guilty Plea of the Purdue Frederick Company and Its Executives for Illegally Misbranding OxyContin, May 10, 2007; U.S. Department of Justice, Statement of United States Attorney Michael Mukasey and Acting United States Attorney Laurie Magid on the $425 million settlement for off-label drug marketing of Actiq, September 29, 2008. https://www.justice.gov/sites/default/files/civil/legacy/2014/01/09/Cephalon%20Press%20Release.pdf (last accessed January 19, 2019).

[228] ENDO-CHI_LIT-00547543 at p. 17; ENDO-CHI_LIT-00023299, p.38,59, Opana Brand Situation Analysis, Laurie Blunt, May 2008; ENDO-CHI_-LIT-00150080.

[229] ENDO-CHI_LIT-00547543 at p. 17.

time, HCPs who were surveyed continued to view "low abuse potential" as an advantage of Opana ER.[230]

119. In addition to qualitative marketing research, Defendants identified and disseminated research and other work that supported their desire to promote opioids as safer and better for treating pain than existing treatments. One study, frequently cited by Defendants in marketing materials, was authored by an industry supported opioid expert, Dr. Russell Portenoy,[231] which concluded, based on research with 38 patient cases, that *"…opioid maintenance therapy can be a safe, salutary and more humane alternative to the options of surgery or no treatment in those patients with intractable non-malignant pain and no history of drug abuse."*[232] Another fundamental piece of support for Defendants' claims about the safety of opioids came from a 1980 letter to the editor in the New England Journal of Medicine which concluded that addiction was rare in hospitalized patients with no history of addiction.[233] These and other writings were

[230] ENDO-CHI_LIT-00023394, p.55, Opana ER – Situation Analysis (Marketing Science) Cassie Mapp, June 2009; ENDO-CHI_LIT-00012061, p.37, Opana ER Customer Satisfaction, Sales Force Effectiveness, Awareness & Usage, Adelphi, January 2010.

[231] Dr. Portenoy consulted with and received grants from pharmaceutical companies. His work was used to support Defendants marketing efforts and messages. These relationships represent the potential for conflicts of interest. See also, e.g., ACTAVIS0685080 and ACTAVIS0685082, in conjunction with Altier_Allergan Deposition pp.269-284. Krishnaraj_Insys Deposition, pp.279-280; Moskovitz_Janssen Vol.1 30(b)(6), KOL and advisory boards pp.80-82, 218-223; Riddle_Purdue Deposition pp.107-108, 289,320,340; Spokane_Teva pp.40-41, 93-98, 264-266; Vordestrasse_MNK p.200.

[232] Portenoy R and Foley K. Chronic use of opioid analgesics in non-malignant pain: Report of 38 cases. Pain 1986; 25:171-186.

[233] Porter J. Addiction rare in patient treated with narcotics. New England Journal of Medicine 1980; 302:123.

cited and disseminated as evidence to support Defendants' claims and notions of opioid safety.[234] [235]

C. Defendants' Marketing Strategy for Opioids

120. In my analysis of Defendants' marketing of opioids, I reviewed many marketing and business documents. The examples that I have cited in my Report are representative of the larger set of documents I have reviewed. Further, the documents cited reflect the activities commonly used by pharmaceutical marketers and provide ample insight into Defendants' marketing activities. The marketing documents I reviewed were developed for use nationally and in Ohio.[236]

[234] See e.g., JAN-MS-00653426, pp.25,36; JAN-MS-00310473; JAN-MS-01257946; JAN-MS-01378537 and JAN-MS-01378536, IMPACT publication, and email regarding tapentadol professional education message platform; JAN-MS-00339425, tapentadol unbranded message platform, and email JAN-MS-00339422; JAN-MS-00653426, Chronic Pain: Prevalence and Impact; JAN-MS-00310473; MNK-T1_0001279950, Coviden Train the Trainer; MNK-T1_0001125603, Train the Trainer; PDD8023055639; PKY180123095; PKY181135768; PDD8023055742; PURCHI-000816988; PKY180111590; Riddle_Purdue Deposition pp.195-197, 208-215 (I got my life back video – PKY180164757), 231, 251-256 (Exhibit 33); Moskovitz_Janssen Deposition Vol.2, 30(b)(6) pp.700-710, 747-759.

[235] PKY18185576, Sample Script for Media Follow up Call; PKY183196681, Purdue Pharma L.P. Statement of Diversion and Abuse of OxyContin. This document summarized many of Purdue's outreach regarding opioid abuse, including work with state medical boards, professional associations, brochures to pharmacies and healthcare professionals, educational programs, etc.; PKY181941506, letter to field sales personnel – material intended for verbal communication by sales personnel; Other sales training and scripts are identified in Schedule 11.

Dr. Portenoy consulted with and received grants from pharmaceutical companies. His work was used to support Defendants marketing efforts and messages. See e.g., ACTAVIS0685080 and ACTAVIS0685082, in conjunction with Altier_Allergan Deposition pp.269-284. Krishnaraj_Insys Deposition, pp.279-280; Moskovitz_Janssen Vol.1 30(b)(6), KOL and advisory boards pp.80-82, 218-223; Riddle_Purdue Deposition pp.107-108, 289,320,340; Spokane_Teva pp.40-41, 93-98, 264-266; Vordestrasse_MNK p.200.

[236] See e.g., PURCHI-000007950, p.6, Sales Training; Altier Deposition p.356; Burbs_Janssen Deposition pp.123-125; Deem_Eshleman_Janssen pp.45-47,55, 129, 137-140; Vorderstrasse_MNK Deposition pp.270, 282-284; Webb_MNK Deposition pp.75-77; Gilliwa_MNK Deposition p.323; Krisihnaraj_Insys Deposition p.277 and Exhibit 5; Snyder_Allergan Deposition p.271; Vitanza-Squires_Endo Deposition p.287-289; Wickline_MNK Deposition pp.76, 90-91, 196-198, 328; Jackson, R_Endo Deposition pp.186-187; Cramer, Phil_11-20-18 Deposition (Purdue), pp.150, 163; See also, Schedule 9: Manufacturing Defendant Testimony that Marketing Plans were National.

121. Defendants worked to create aggressive[237] marketing strategies for opioids which served to distort needs, wants, and demand for opioids. Evidence that Defendants' marketing was aggressive is seen in marketing and brand plans,[238] tactical plans, sales training[239], and other documents and communications cited throughout this Report.[240] [241] [242] [243]

[237] The term aggressive, from a marketing perspective, refers to how vigorously marketing strategies are developed and implemented.

[238] See Schedule 8: Manufacturing Defendant Marketing Plans.

[239] See Schedule 11: Manufacturing Defendant Sales Training Manuals and Scripts.

[240] See e.g., EXALGO Fast Start Challenge Reward Trip Follow-Up, Mallinckrodt-Wickine-006; Mallinckrodt-Wickline-007. 30300-Ohio Business Plan "Go Where You Can Grow"; Mallinckrodt-Wickline-009, Dean February 1, 2013 email with subject: National Successes and what YOU can do to drive Q@***Action Required***; Mallinckrodt-Wickline-015, Sales Force Effectiveness, Tsunami Launch, "Blitz" of pharmacies and physicians, p.E0501.78-80; Glenn August 13, 2008 email addressed to "Pittbulls", EPI000882976; "Tsunami Launch Plan!", Endo Pharmaceuticals Inc, June 2002, Mallinckrodt-Wickline-014; Mallinckrodt-Wickline-018, Wickline October 18, 2006 email with subject: RE: Sharp Stick Notes – IMPORTANT Read promptly, citing 20,440 presentations to 5,222 docs in decile 7-10; Wickline-Mallickrodt-019, Project Sharp Stick, "We aren't changing the plan one bit, just implementing it with more intensity and focus for maximum effect"; Jolliff_MNK Deposition pp.129-138 and Jolliff_MNK Exhibit 6.

[241] There was also pressure on sales reps to push higher dosage formulations, see MNK-T1_0000754771 (sales report demonstrating physician targeted to prescribe Exalgo in doses that exceeded 200mg morphine equivalent); ALLERGAN_MDL_01112579 (Patient Adherence Program to improve persistence and increase overall length of therapy).

[242] One document that informed my opinion of aggressive marketing was the 2014 Purdue BDC – Project Tango presentation. In this presentation, Purdue outlines strategy to acquire "Tango," referred to as a leader in addiction treatment. The strategic rationale for this proposal was that Purdue could become and "end-to-end pain solutions provider" (PPLPC016000255303, BDC meeting – Project Tango, p.14) implying Purdue could treat pain and then treat the addiction that can result from pain treatment. The presentation notes Tango has a pipeline, including, e.g., Naloxone Intranasal Spray. This presentation lays out Purdue's core capabilities, including leveraging its marketing to educate and de-stigmatize addiction, utilizing KOLs, employing FDA and payer relationships to drive a clinical paradigm shift in addiction and other actions. Purdue forecast that Tango could represent over 50% of its sales by 2023 providing insight into the magnitude of the addiction treatment market. This example provides insight into how aggressively Purdue sought to engage and dominate the opioid market.

[243] Defendants also created audio/video marketing pieces intended for a variety of internal and external audiences. For at least some of these video productions the tone is quite commercial. See e.g., JAN-MS-04212484, Dr. Rosenbery / Nucynta; JAN-MS-04213835, Dr. Pergolizzi / Nucynta ER; JAN-MS-04212411, Dr. Fine / Nucynta; JAN-MS-04212293, Dr. McCarberg, unbranded message; JAN-MS-0390726, Dr. Twillman (PhD, policy and advocacy director, AAPM; JAN00008022 (Peer-to-peer online program offering); JAN00009001; JAN00130397; JAN00131350; JAN-MS-02364493; MNK-T1_0007029131 (Propah Dose rap lyrics excerpt: "So when you start at the middle or you start at the top or you start with a little, make sure you just don't stop. (Why? Wha' ya' mean?) 'Cause yah' patient need relief, mon! So do what you should. When you convert and titrate, hahahaha make sure….it's all good! Oh! It's all good! Oh! It's all good! Oh! It's all good! Good good, it's all good. You got to have a propah dose, mon. Titrate. The

122. Defendants' aggressive[244] marketing put patient welfare at risk through increased prescribing of opioids. The Defendants' marketing strategy for opioids was designed to turn drug features into drug benefits, create desirable positioning in Customers' minds, and stimulate prescriptions for opioids. Each of these activities is consistent with marketing principles, but not with industry standards for the marketing of dangerous drugs like opioids.

Marketing Information Bias Toward Benefits, not Harms

123. It should be noted that Defendants' marketing documents sometimes reference the need to disclose safety information for drugs, consistent with FDA-approved indications and prescribing information contained in the PI.[245] In one Kadian plan, PSRs were specifically directed to discuss safety considerations with prescribers during sales calls.[246] However, the preponderance of

propah dose. Exalgood. Exalgood. It's Exalgood.); MNK-T1_0006835316 (audio, When Less is More); MNK-T1_0007033463 (The interesting physician parody, stay focused my friends); TEVA_MDL_A_00717855 (Actiq sales training); TEVA_MDL_A_00715630 (News clips); TEVA_MDL_A_00717114 ("Doug" a construction worker); TEVA_MDL_A_00717111 (Converting Actiq prescribers); TEVA_MDL_A_00717116 (Actiq v Fentora); TEVA_MDL_A_00717117 (Pain Lingers); TEVA_MDL_A_00717110 (Patient and Doctor, BTP).

[244] Reference is also made to aggressive marketing by Defendants and others, see e.g., Riddle_Purdue Deposition pp.33-34, 134; Wickline_MNK Deposition p.147; OxyContin Launch Plan, 1995, PURCHI-003286149; 2013 Preliminary Business Plan, July 31, 2012, JAN00019880; Cohen, June 28, 2011 email with subject: Oxymorphone ER 7.5mg & 15 mg, ALLERGAN_NDL_00132475; Covidien Pharmaceuticals Internal Newsletter Article, April 26, 2010, Pennsaid and Exalgo, MNK-T1_0000857461; Burlakoff October 2, 2013 email, INSYS-MDL-000392811; ENDO-OPIOID_MDL-00439663; Mallinckrodt-Wickline-008, Meyer May 30, 2013 email with the subject FW: Operation Change Agent; MKN_TNSTA00311798, "Meanwhile, pill manufacturers launched aggressive marketing campaigns promoting the drugs." "At around the same time, the companied that manufactured these narcotics – including Purdue Pharma, Johnson & Johnson, and Endo Pharmaceuticals – began to aggressively market their products for long-term, non-cancer pain, including neck and back pain" In Mallinckrodt-Wickline-023; Van Zee, A. The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy. Am Journal of Public Health, 2009; 99(2): 221-227; Key Strategic Imperative: Customer-Facing Organizational Readiness, p.2, MNKT-T1_0000184758; Exhibit Endo-Chapman-6, Statement of Unites States Attorney John Brownlee on the Guilty Plea of the Purdue Frederick Company and its Executives for Illegally Misbranding Oxycontin; Note: Mr. Gasdia at Purdue did not personally agree with this characterization of Purdue's marketing, yet, described efforts that fit a marketing definition of aggressive marketing (Gasdia_Purdue pp.126-136).

[245] While cautionary statements were noted in the PIs of all Defendants, as noted above, the PI is not generally relied on in personal selling situations. See also e.g., Cycle 1 Meeting, Training Workshops, JAN00085130, for a slide entitled: "Compliance is Essential."

[246] See also, e.g., Kadian 2011 National Sales Meeting, "Putting it all together," 132_ACTAVIS0413281, Do's and Don'ts.

Defendants' messages (discussed in detail below) focused on translating drug features into drug benefits, and downplayed information that would serve to discourage prescribing, including potential harms.

124. Like the Kadian plan, in a 60-slide sales training presentation for Nucynta, Janssen notes at the outset that PSRs should always "disclose safety information for all company-promoted products." This is the only mention of safety in this presentation; yet, there is ample content instructing PSRs on how to communicate drug benefits, including copay cards and other selling messages. The "core" messages in this presentation include: "Powerful Efficacy, Favorable Tolerability & Discontinuation Rates, Mechanism of Action, Dosing and Titration, Access and Affordability."[247] Other Janssen programs provided similar training themes with a focus on benefits and selling, not on reasons to be cautious or to choose a non-opioid alternative.[248]

125. In a different kind of example, David Horton, a Product Manager from Mallinckrodt, was asked to identify key talking points for an upcoming meeting where face-to-face promotion of Xartemis, an extended-release oxycodone/acetaminophen, would occur. If the company's focus was to always provide a balance of information on the benefits and harms, it is certainly not reflected in this communication. Mr. Horton's list of talking points included: "*set up the unmet need; establish a specific patient appropriate for XARTEMIS XR; Sell the benefits of IR AND ER – fast acting/long lasting; promote the impact of simple, twice daily dosing; and, close to action with specific patients."* In the narrative and instruction provided in this instance, no mention of any cautionary information is made.[249] In another Mallinckrodt sales leadership training for Xartemis, which included multiple training objectives, there is no training related to the dangers

[247] Retail Training Workshop, JAN00089339.

[248] See e.g., Retail Training Workshops, JAN00079899. There were other similar presentations related to Institutional sales, such as JAN00081397.

[249] 20_MNK-T1_0000130448, 2/19/2015 email with subject, RE: ECRM.

of opioids (harms), only training on how to achieve sales objectives such as "more rapid and sustainable sales."[250]

126. The FDA warning letters cited above also support the proposition that Defendants minimized risk information in their marketing. These letters describe the FDA's position on certain marketing for MS Contin, Duragesic, Avinza, Fentora, Ultram, Embeda, Kadian, and Nucynta.

127. Defendants also expressed views related to the communication of risk information about their drugs. For example, Mr. Bingol, a former Senior Director of Marketing at Endo who had responsibility for Opana and Opana ER, was asked about the issue of the history of abuse of oxymorphone. According to his testimony, Endo promoted the drug in accordance with its label, but never provided education to its sales force, health care providers or patients about history of abuse of oxymorphone pills.[251] Mr. Romaine, a former Vice President of Sales at Endo confirmed PSRs spent most of the time during their sales calls discussing the "features and benefits" of the products and did not, for example, review the black box warnings verbatim during their sales calls.[252]

128. Mr. Boyer, former President and CEO of Teva, testified that using sales representatives to communicate with doctors about the proper use and risks of opioids was cost prohibitive and not done by Teva. He further indicated that other, less costly ways of communicating this information were also not used by Teva.[253] Mr. Webb, testifying for Mallinckrodt, was asked about risk information related to addiction in marketing materials. He stated, *"—refresh my memory on what we consider the fair balance in the important patient risk information that we put on our material. But I know that we share with the physician, anytime opioids were being*

[250] 23_MNK-T1_0000132919, Field Sales Tactical Brand Planning.
[251] Bingol_Endo Deposition pp.334-340 and Exhibit 36.
[252] Romaine, Larry_Endo Deposition pp. 501-503.
[253] Boyer_Teva Deposition pp.317-320.

discussed in our promotional material, that there is a risk of addiction. The degree of that, I can't speak to."[254]

129. A heavy emphasis on persuasive selling techniques also propelled Defendants to focus on benefits over risks (discussed in Section III below) in order to increase awareness of core messages and generate prescriptions. In fact, when it came to communication of some of the most significant potential harms stemming from opioid use, PSRs were instructed not to initiate discussions with Customers on these issues (diversion, abuse, dependence, tolerance, or addiction). When these subjects were brought up by Customers, PSRs were taught to *"[r]e-focus to the true pain patient and then sell."*[255]

130. Other sales training documents also contained evidence of aggressive sales techniques. For example, Purdue PSRs were taught to use effective sales techniques focused on changing Customer behavior through role-play scenarios.[256] In one such scenario, the physician is objecting to converting an NSAID patient to a 7-day transdermal opioid. Purdue PSRs are taught to challenge the objection with responses aimed at convincing the doctor to prescribe Butrans, specifically:

> **"[Scenario]** ***4. After conducting multiple calls, Dr. Simpson (Internal Medicine) has yet to prescribe Butrans. During a recent discussion he mentioned, "I would not convert from an NSAID to a 7-day transdermal opioid." After presenting the key attributes for Butrans, select the best powerful question to ask the HCP:***
>
> *A. "Doctor, you have already said that you would prescribe Butrans. What is getting in the way of selecting an appropriate patient for Butrans?" Listen to HCP response and then deliver an appropriate closing statement.*
> *B. "Why haven't you initiated Butrans?" Listen for response, revisit the attributes, and close on managed care coverage. "Doctor, knowing the coverage for Butrans has expanded to plans in your practice will you prescribe this week?"*

[254] Webb_MNK 30(b)(6) pp.143-145.

[255] PPLPC012000018382, Managers Meeting Workshop III, Handling Abuse, Addiction and Diversion Issues in a Selling Situation. *See* also 2011 Opana ER New Objection Handler, END00195234 (explaining standard response to objections about potential abuse of Opana ER); 2007 Endo Example ECR, ENDO-OPIOID_MDL-00774115 (example PSR coaching report; in response to provider concern about potential abuse, PSR responds that he has not heard of cases of abuse of Opana).

[256] PPLP003288099, September 2016 Pre-POA Test.

C. "I realize that insurance coverage has been an issue for you in terms of prescribing an extended-release opioid." Focus on Dynamic Access Messaging insurance grid. "Doctor, knowing that Butrans has broad formulary coverage will you prescribe for an appropriate patient?"
D. "Clinically speaking, if you had the opportunity to prescribe Butrans to a chronic pain patient inadequately managed on an NSAID, what would that patient look like?" Listen to gain the HCP's perspective, then say "Describe for me why you would initiate Butrans for this patient type." Listen for response, then ask: "What would the conversation sound like with the patient when discussing your clinical rationale for converting from an NSAID to Butrans?"

131. Endo trained PSRs respond to physician concerns using a technique known as Clarify, Respond, Confirm, and Transition (CRCT).[257] This and other methods taught PSRs to address concerns about abuse with statements that verbally agree with concerns, reframe the issue, and refocus (distract) the prescriber with messages such as, *"Doctor, can I discuss a few key advantages and benefits that OPANA® ER (oxymorphone) may offer those in need of an opioid for moderate to severe pain?"* Further, Endo taught PSRs that *"objections"* are *"opportunities."*[258]

132. Specifically related to the balance between benefits and harms, the examples cited here are representative of other documents in the record. Objection handling and other sales training clearly provided PSRs with effective sales skills; however, the share of voice between benefits and harms was skewed toward benefits. Most of the documents I reviewed provided little or no information on the risks of opioids. When this information was included, it was with respect to how to minimize objections to opioid use.[259] Further, aggressive sales techniques are not appropriate for dangerous prescription medications. At the least, these techniques minimize

[257] https://www.amanet.org/training/articles/i-object-four-steps-to-handling-objections.aspx (last accessed March 11, 2019); Jackson, R_Endo Deposition, pp.326-329, 332-333; Endo also used other persuasive techniques such as "Engendered Thinking"; Jackson, R_Endo Deposition, pp.167-169, 276-277 and Exhibit 16 (ENDO-OPIOID_MDL 02489842), Endosell Training Program: Your Custom Guide for Selling Success, p.6.

[258] See e.g., ENDO-OPIOID_MDL-0279844, Objection Handling Workshop, An objection is an opportunity!

[259] See e.g., ENDO-CHI_LIT-00552370, OPANA ER Managed Care Message Verbalization Workshop; JAN-MS-00129495, Workshop 3: Questions and Concerns, question on serotonin syndrome; ACTAVIS0003698, Responding to Customer Objections – Kadian.

potential harms; at worst, they dismiss safety issues entirely, providing further support for the proposition that Defendants minimized concerns over the use of opioids.

Defendants' Marketing Messages

133. Using the proven marketing techniques described in this Report, the overarching goal of Defendants' marketing was to remove barriers to prescribing opioids and move opioid prescribers from trial to adoption, rapidly and durably.[260] To accomplish these goals, Defendants needed to increase awareness of their drugs and overcome barriers related to prescribing opioids, including:[261]

- redefining who will be treated with opioids;
- destigmatizing opioid use;
- convincing prescribers, payers, and other Customers, that pain should be treated with opioids first, and;
- convincing stakeholders that opioids are less risky, have less abuse potential, and fewer side effects than existing perceptions dictate.

134. Defendants utilized specific marketing messages to accomplish the goals of increasing awareness and removing barriers to opioid use. All of Defendants' messaging can be grouped into three (not mutually exclusive) general themes that worked together to create the new positioning of opioids in Customers minds, namely:

[260] See e.g., PPLPC008000005359, p.3, "Global vision for 2000 and beyond: MS Contin revolutionized how Cancer pain is treated; OxyContin revolutionized how non-cancer pain is treated; Palladone XL will revolutionize how all persistent pain is treated." These statements reflect a future vision of marketers at Purdue with respect to the drug Palladone which was approved by the FDA in 2004. Segment strategies are enumerated.

[261] See e.g., the relevant sections (competitive landscape, SWOT analyses, etc.) of marketing plans cited in this Report; see also, Bennett P 011619 Deposition, pp.126-127; PPLP008000005359 p.44-45; PPLPC012000064369, Business Plan written by Bernie Katsur, Purdue National Account Executive; ACTIQ 2002 Marketing Plan, Pyfer_Teva Deposition Exhibit 18 (TEVA_MDL_A_00454816).

- ***Dependence, tolerance, addiction, and withdrawal should not be a concern in prescribing opioids***. This included messages such as, for example, patients taking opioids for pain do not become addicted; fewer than 1% of pain patients get addicted; pain cancels or prevents euphoria, which is why pain patients do not get addicted; extended release (e.g., q 12 hour dosing) formulations prevent peaks and valleys, which in turn prevents euphoria and addiction; extended release formulations are hard to abuse, so there is no/less danger in prescribing them. Tolerance is not a concern because doses can be increased without limit; withdrawal/physical dependence is not a problem because patients can easily be tapered off opioids and because physical dependence itself does not produce compulsive out-of-control use or other opioid-related problems.

- ***Opioids are effective for, and improve functioning in, patients taking them for long-term and chronic use.*** This theme includes the expansion of the indication for patients who require opioid therapy for "more than a few days" into "chronic use" as well as the claim that there is evidence of improved functioning in patients taking opioids for chronic pain; the omission of side-effects associated with long-term use such as hyperalgesia[262] and sedation.

- ***Opioids should be first-line therapy for pain.*** Using their knowledge of their products and Customers, Defendants turned product features into product benefits by transforming the first two themes into a third: pain should be treated with opioids first. The rationale for this was clear. If addiction, dependence, tolerance, and withdrawal are not concerning, and if opioids make the pain patient's life better, why not start with opioids? This theme also

[262] Hyperalgesia is an increased sensitivity to pain which can be caused by exposure to opioids. It is paradoxical that patients treated for pain may become more sensitive to pain. Hyperalgesia can be treated by reducing opioid dosage or tapering the opioid dose. Lee M, Silverman S, Hansen H, Patel V and Manchikanti, L. A comprehensive review of opioid-induced hyeralgesia. Pain Physician. 2011;14(2):145-61.

included the comparative messages that other drugs to treat pain, namely NSAIDS, are dangerous to use.

Using these three themes, Defendants' marketing changed the face of pain therapy in the U.S. by re-positioning these drugs in Customers' minds.

Theme One: Dependence, tolerance, addiction, and withdrawal should not be a concern in prescribing opioids.

135. One of the barriers to opioid prescribing has been the potential for, and fear of, addiction. Numerous marketing messages used by Defendants' communicated information that supported a change in the paradigm regarding the link between addiction and opioids.[263] [264] Examples of these messages are provided in Table II: Marketing Messages, and include:

- Janssen's internal sales materials for Duragesic that stated *"[p]hysicians should not let concerns of physical dependence deter them from using adequate amounts of opioids in the management of severe pain when such use is indicated"* and claimed a lower abuse potential for Duragesic;[265]

[263] See Table II: Marketing Messages and Schedule 10: Marketing Messages.

[264] Sales personnel were trained on how to handle objections to multiple issues including concerns over addiction. See e.g., Kadian Objection Handler, ACTAVIS0003698; 0a8_ACTAVIS0829193; Objection Handling Workshop, ENDO-OPIOID_MDL-02489844; Taking Aim at Objections, Combunox, ALLERGAN_MDL_03502668; ENDOSell™ Objection Handling, ENDO00023594 in Opana ER Competitor Knowledge Product and Therapeutic Learning System (Sales Training and Development, April 2009) ENDO00023515; Revopan™ Workshop, December 9, 2010, ENDO-CHCI-LIT-00053081; Delivering the Difference, ENDO-CHI_LIT-00166509; Field Coaching Report, Kristiana Wright DSM, INSYS-MDL-007215874; BRM Training, INSYS-MDL-008344022; (Sales) Training Progress Report, JAN00068321; Xartemis XR BroadcastScript March 17, 2014, MNK-T1_0000702315; Delta Point, Inc. Proposal for Pennsaid and Exalgo, MKNK-T1_000094043; September 25, 20000 Memo, November 13, 2000 Phase II Training Program, E16_00002947; Workshop 6: REV it Up! Nucynta National Meeting, JAN00047720; Managers Meeting 2007, Sales Training, TEVA_MDL_A_00358559 (focus on managed care); Fentora Training, TEVA_MDL_A_00359511.

[265] See JAN-MS-01192118 (2001 Product New Update: Addictive Nature of Opioids).

- Mallinckrodt's communication of the message that MNK-795 (oxycodone/APAP extended release), "provides fast-acting and long-lasting relief without concerns about abuse;"[266]

- Purdue messages that "Copious evidence that the proper use of opioid medication for pain relief does not make patients vulnerable to addiction,"[267] "The fact is, no one today has to suffer in pain, because effective medications, like opioids, are available and patients rarely become addicted or tolerant to opioids,"[268] and "Tolerance & physical dependence with opioid analgesics are not indicative of addiction... Addiction is a purely psychological disorder... Opioid tolerance is good. Odds of addiction in non-addicts from lawfully prescribed medications is 1/800 to <1/10,000."[269]

- Endo's launch of the "Think Opana" campaign built on market research that providers preferred hearing that a product was "less risky" and reported a sense of "calm" in response to messages conveying a product was "simple."[270] "[T]reats the pain and not the addiction."[271]

- "The National Institute on Drug Abuse has said that most patients using opioids for pain do not become addicted," and "Physical dependence and tolerance are

[266] 39_MNK-T10000228064 p.26, with a strategic imperative (p.27) to "Differentiate NMK 795 from the competitors on the merits of the brand based on analgesic performance and abuse deterrence. This compound would come to market as Xartemis.

[267] PKY180425172, Partners Against Pain Professional Education, 1998, Purdue information for Medical Professionals. Extensive information which Includes the AAPM and APS Joint Consensus Statement on Opioids for Pain Control.

[268] PPLPC009000006347, 1999 Pain Backgrounder. "Pain Exacts a Heavy Toll." Includes citation to Porter and Jick.

[269] PKY180775599, Accredited Pain management Program for the Educator, 2000, Approved for continuing education for pharmacists and nurses.

[270] 2008 Opana Brand Situation Analysis ENDO-CHI_LIT-00023299.

[271] EndoSell Coaching Report, Brandon Myers, 2006, ENDO-OPIOID_MDL-00678171.

normal physiological consequences of extended opioid therapy for pain and should not be considered addiction."[272]

136. Other marketing messages claimed patients with legitimate pain cannot become addicted because their pain protects against addiction.[273] Defendants also taught Customers that when the signs of addiction are present, it is just a symptom of undertreated pain or "pseudoaddiction,"[274] and the solution to pseudoaddiction is to prescribe more opioids.

137. Fears were also minimized through marketing communications that indicated problems like addiction occur only when opioids are abused or used illegally,[275] and if opioids are taken as

[272] ABT-MDL-KY-0012834; OxyContin Talking Points Binder.

[273] PKY180625450 – "Iatrogenic 'addiction' to opioids legitimately used in the management of pain is very rare."; "Key Selling Points – Patient Care – Opioid Analgesia an Essential Tool in Chronic Pain, by Dr. Neil Ellison: "Page 3, Physical dependence is an unavoidable pharmacologic response to prolonged therapy, addiction is very rare." This is a tool that can be used to overcome Dr. misconception of opioids and addiction. Can lead into discussion on key terms of tolerance, addiction, dependency, pseudoaddiction, Etc. Good source to show that less than 1% of patients become addicted. It can also be pointed out that pain specialists strongly advise the use of opioids." E01_00015979; PKY180504210.

[274] PKY180170528 – "Pseudo-addiction is not a diagnosis but a predicament due to under-medication for pain; it consists of being misdiagnosed as having a substance abuse disorder because of the resultant drug-seeking behavior." "Suggested diagnosis test of pseudoaddiction: prescribe a substantially increased dose of opioid so the patient can explore the optimum dose."; PPLP003517021 – "Pseudoaddiction is a term which has been used to describe patient behaviors that may occur when pain is undertreated. Patients with unrelieved pain may become focused on obtaining medications, may "clock watch," and may otherwise seem, inappropriately "drug seeking."; Key Selling Points – Patient Care – Opioid Analgesia an Essential Tool in Chronic Pain, by Dr. Neil Ellison: "Physical dependence is an unavoidable pharmacologic response to prolonged therapy, addiction is very rare." (<1%) E01_00015979; Assessing the Risk for Substance Abuse, JAN-MS-00310473; PKY183146275; PKY180123095 (Partners Against Pain publication); MNK-T1_0001028027 at pp. 26, 34 (Exalgo training module citing pro-opioid scientific papers, such as AAPM/APS, Fishman, Portenoy, Chou, including reliance on pseudoaddiction theory); ENDO-CHI_LIT-00538705 (training module describing pseudoaddiction as drug-seeking behavior that only mimics addiction but is resolved by giving the patient more drugs).

[275] See generally, e.g., "Proper assessment of patients, proper prescribing practices, periodic re-evaluation of therapy, and proper dispensing and storage are appropriate measures that help to limit abuse of opioid drugs." Fentora Frequently asked questions and responses. TEVA_CHI_00000509, p.11; "…opioid agonists are sought by drug abusers and people with addiction disorders and are subject to criminal diversion. These risks should be considered when prescribing or dispensing KADIAN in situations where there is concern about increased risks of misuse, abuse or diversion. Concerns about abuse, addiction, and diversion should not, however, prevent the proper management of pain." KADAIN PI Workshop, ACTAVIS0567695, p.17; PKY180775599 – "Pseudoaddiction: (p.51, 73). Odds of addiction in non-addicts from lawfully prescribed medications is 1/800 to <1/10,000"; PKY180504210, "Fears about

prescribed, the risk of addiction is rare (less than 1 percent).[276] Defendants further downplayed addiction by carefully defining the terms "tolerance" and "pseudotolerance" to justify marketing the highest doses of opioids to patients.[277] According to Defendants' messaging, each of these conditions has a common solution: taking higher doses of opioids.[278] As late as 2016, Defendants were still training sales personnel to minimize addiction concerns by blurring the terms "drug abuse," "drug addiction," and "dependence" and continuing to suggest that a physically-dependent patient cannot be addicted to an opiate if that patient experiences pain.[279]

psychological dependence are exaggerated when treating appropriate pain patients with opioids."; Direct to customer marketing for patients ("Living with chronic pain – Your guide to better days and night", from the makers of Avinza® 24 hour (morphine sulfate extended-release capsules), END00014045, p.5; "Some people abuse opioids. This means they use the drug to get "high," not for pain relief. This drug-seeking behavior is continued despite harm or risk of harm." "Under proper medical supervision, the risk of opioid addiction is low." END00014029.

[276] See generally, e.g., "long history of safety and efficacy when used as indicated" Kadian Marketing Overview, ACTAVIS0264972, p.31; "risks can usually be managed" ENDO-CHI_LIT-00549936, p.3; PDD8023045826 "Addiction is rare in the physically dependent patient."; Key Selling Points – Patient Care – Opioid Analgesia an Essential Tool in Chronic Pain, by Dr. Neil Ellison, (tolerance, addiction, dependency, pseudoaddiction) E01_00015979; PKY180504210 "Addiction risk also appears to be low when opioids are dosed properly for chronic, non-cancer pain"; PKY180425172 "Copious evidence that the proper use of opioid medication for pain relief does not make patients vulnerable to addiction"; ALLERGAN_MDL_00405512; ABT-MDL-KY-0012834; ENDO-CHI_LIT-00551655; ENDO-CHI_LIT-00552471.

[277] See PKY183146275 at 8-10; see also PPLP004085756 at p. 2. This targeted selling to physically-dependent opioid-treated patients was seen in sales evaluations, where PSRs are criticized for not expanding sales of higher-dose OxyContin for patients already prescribed at highest doses.

[278] See E01_00012535, p. 10, "Fortunately, opioids do not have a ceiling effect and if tolerance occurs, the dose may be increased to maintain pain relief"; See Schedule 10.

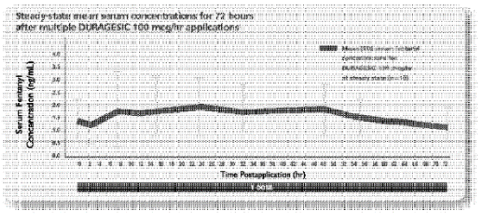
[279] See PPLP003572026 ("Is it Pain? An educational offering from Purdue Pharma L.P.").

TABLE II: Marketing Messages

A. Extended release drugs and/or q12 dosing- had fewer peaks and valleys and less chance of addiction and abuse.

Bates	Date	Contents	Defendant
http://www.painmed.org/2015-posters/abstract-213/	2015	Presentation at 2015 American Academy of Pain Medicine Annual Meeting, with a MNK sponsored study about the comparison between Immediate Release (IR) / Extended Release (ER) hydrocodone bitartrate / acetaminophen combination drugs, and IR hydrocodone bitartrate / acetaminophen combination drugs. Results of the study are that single, equal, oral doses of IR/ER HB/APAP drugs showed lower abuse potential as measured by drug liking, high, and good drug effects, over IR HB/APAP, whether intact or crushed.	Mallinckrodt
ACTAVIS0335094	11/2011	Regional Meetings November 2011 "Kadian provides steady blood levels of morphine sulfate with few peaks and valleys."	Allergan
ALLERGAN_MDL_00638086	2/18/2010	DDMAC Warning Letter: "Unsubstantiated Superiority Claims… 'Fewer peaks and valleys. Smooth steady-state plasma levels compared with controlled-release (CR) morphine tablets q12h and q24h…" (Kadian Comparison Detailer)	Allergan
ALLERGAN_MDL_01290412		Kadian Comparison Detailer cited in DDMAC Warning Letter Fewer peaks and valleys. Smooth steady-state plasma levels compared with controlled-release (CR) morphine tablets q12h and q24h	Allergan
ACTAVIS0000564	03/2013	Kadian Sales Training Presentation	Allergan
ACTAVIS0006930	2005	2005 Publication Plan Discussion of drugs and mentions PK profiles/peaks and troughs, "Current Promotional Tagline – Kadian provides consistent pain relief without the peaks and valleys."	Allergan
ALLERGAN_MDL_00001525	02/2013	Steady blood levels with few Peaks and valleys	Allergan
ALLERGAN_MDL_00072907	9/13/2012	Kadian produced higher trough concentrations and a smaller degree of peak-to-trough fluctuations	Allergan

ALLERGAN_MDL_00405512	7/30/2010	Few peaks and valleys	Allergan
PPLP003397245	4/9/15	"The PK graph shows Hysingla ER plasma concentrations at steady state delivering hydrocodone over a 24 hour period with every 24-hour period with every 24-hour dosing for 3 days."	Purdue
ENDO-CHI_LIT-00550036	11/2/15	"The original formulation delivered consistent plasma levels that lasted with low peak and trough fluctuations through 12 hours."	Endo
ENDO-CHI_LIT-00012014		"Stable steady state plasma levels over the entire dosing period- so you can have the confidence of true 12 hour dosing."	Endo
PPLP003288099	9/1/2016	"One Hysingla ER tablet taken at the same time each day will provide your patients with around-the-clock hydrocodone delivery. Recall doctor, the appropriate patient we're discussing is no longer adequately controlled on their current around-the clock opioid therapy, correct?" Listen for response, and say: "You're looking for an option for this patient. Let's review the clinical reasoning as to why Hysingla ER may be an appropriate option for this patient." p. 3	Purdue
PPLP003456949	6/12/15	"The PK graph [Section 12.3] shows Hysingla ER plasma concentrations at stead state delivering hydrocodone over a 24 hour period with every 24-hour dosing for 3 days. The delivery of hydrocodone depicted in this graph does not equate to efficacy over the 24-hur period, however, the clinical trial showed that Hysingla is efficacious in a 24-hour regimen."	Purdue
PURCHI-000622986	1/11/1996	"Convenient q12 schedule won't interfere with patients daytime activities or nighttime rest, and encourages compliance." p. 68	Purdue
PPLP03998251	12/31/1999	"Q12h dosing provides smooth and sustained blood levels- fewer peaks and valleys than with immediate-release oxycodone."	Purdue
ENDO-OR-CID-00915135		"Proven and sustained oxymorphone blood levels for a full 12 hours."	Endo
PKY180704970	11/3/1997	"q12h dosing provides smooth and sustained blood levels – fewer peaks and valleys than with immediate-release oxycodone"	Purdue
ENDO-CHI_LIT-00417068	09/2012	"Has better 12-hour efficacy, with true 12-hour dosing, a crush-resistant formulation	Endo

		that minimizes abuse potential, and fewer drug-drug interactions compared with other pain therapies in the class."	
ENDO-CHI_LIT-00150080	11/5/07	"Main message was 24-hour efficacy with less peaks and valleys, less breakthrough pain."	Endo
ACTAVIS0795954	2012	KADIAN may be less likely to be abused by health care providers and illicit users for the following reasons[2]: • Slow onset of action • Lower peak plasma morphine levels than equivalent doses of other formulations of morphine • Long duration of action • Minimal fluctuations in peak to trough plasma levels of morphine at steady state	Allergan
JAN-MS-00299212	2004	Long-lasting efficacy Up to 72 hours of uninterrupted pain relief per patch Provides fewer peaks and troughs Consistent drug delivery over 3 days 	Janssen
PKY180266088	6/30/1999	"Use of longer-acting medications, such as methadone, controlled-release morphine / (oxycodone), could theoreticalyl avoid such withdrawal phenomena by providing continous, relatively stabel blood plasma levels of opioids."	Purdue

B. Abuse deterrent formulations deter abuse.

Bates	Date	Contents	Defendant
MNK-T1_0000115443	09/30/2013	Fingerpaint (3rd party marketing agency hired by MNK to prepare for launch of Xartemis) presentation includes the following value proposition for Xartemis: "Abuse deterrent qualities that make it more difficult to tamper the product and result in reduced drug high, drug liking, and fewer good drug effects that make the product less desirable for abuse"	Mallinckrodt
MNK-T1_0000117111	08/12/2013	Email from Sanjeev Luther, VP Global Business Insights and Forecasting, to the marketing / sales team with similar message	Mallinckrodt

		about Xartemis: "The drug is also formulated with abuse deterrent properties including tamper resistance, and the profile is less-liked by recreational drug abusers due to the controlled release, which makes it a potentially less abusable alternative to Percocet and Oxycontin."	
ACTAVIS0006930	2005	2005 Publication Plan "Remoxy … incorporates several abuse-deterrent properties…Tests indicate that crushing or physically manipulating Remoxy does not defeat its long-acting mechanism."	Allergan
JAN-MS-00259893	6/13/2003	"only AP-48 combines the superior potency of fentanyl with naltrexone in a proprietary formulation to safeguard against unintended usage"	Janssen
PPLP003287356	8/30/2016	"Tell Dr. Hardy that Nucynta ER does not have the same abuse-deterrent formulation as OxyContin and explain the differences."	Purdue
PPLP003397245	4/9/15	"The in vitro data demonstrate that Hysingla ER has physical and chemical properties that are expected to deter intranasal and intravenous abuse." "As not all patients respond in the same way to, or can tolerate, a particular medication, it is important that healthcare professionals have an array of treatment options, ideally with some abuse-deterrent characteristics."	Purdue
PPLP003456949		"Based on the invitro and clinical abuse potential studies, Hysingla ER is expected to deter intranasal and intravenous abuse and oral abuse when chewed." "Purdue recognizes the abuse of prescription opioid analgesics is a significant public health problem, which is why it is important that physicians have more treatment options with abuse-deterrent characteristics.	Purdue
PURCHI-000007950	9/24/2015	"OxyContin and Hysingla ER may be described as having 'abuse-deterrent characteristics or properties' expected to reduce abuse by injection or intranasal routes."	Purdue
ENDO-CHI_LIT-00417068	9/2012	"The ideal therapy for chronic pain consistently provides effective pain relief	Endo

		over the entire dosing interval and offers minimal side effects, drug interactions, and potential for abuse, misuse, and diversion." "Has better 12-hour efficacy, with true 12-hour dosing, a crush-resistant formulation that minimizes abuse potential, and fewer drug-drug interactions compared with other pain therapies in the class."	
ENDO-CHI_LIT-00556061	01/2010	"Low abuse potential is the greatest benefit of a tamper resistant formulation,"	Endo
END00553151	4/5/2011	"Endo has in development a new oral tamper resistant formulation of long-acting oxymorphone (Opana ER), which is designed to be crush-resistant. This new formulation is being developed in an effort to make available to patients and prescribers a product that may provide an incremental barrier to certain types of misuse and abuse."	Endo
PPLP003299511		"Results support that, relative to original OxyContin, there is an increase in the ability of OxyContin to resist crushing, breaking, and dissolution using a variety of tools and solvents."	Purdue
ENDO-CHI_LIT-00044922	2/26/2010	"EN3288, with all of its hard tablet and pharmacological properties, can impact each link of what I dubbed the 'abuse migration' chain. Through this visualization, it is easy to see how, conceptually, all of the qualities of the product can have an impact on the each step of the abuse migration path, save the kitchen chemist who will likely take any challenge as far as they can."	Endo
PPLPC012000018382		"Delayed absorption, as provided by OxyContin tablets, is believed to reduce the abuse liability of the drug."	Purdue
ENDO-CHI_LIT-00417068		"Has better 12-hour efficacy, with true 12-hour dosing, a crush-resistant formulation that minimized abuse potential, and few drug-drug interaction compared with other pain therapies in the class." "true 12 hour dosing and a crush-resistant formula that minimized potential for abuse, misuse, and diversion."	Endo

PDD1502310593	4/30/1999	"Neither of these oral agents can be readily dissolved in saline or other diluent and administered as an injection. Additionally, if either agent is put into a solution and injection is attempted, the occurrence of a necrotic lesion at the injection site is a powerful impetus to stop this practice." (p. 5)	Purdue
PPLP032000397039	2017	"In Vitro data demonstrate that OxyContin has physicochemical properties expected to make abuse via injection difficult." "Data from a clinical study, along with support from the in vitro data indicate that OxyContin has physicochemical properties that are expected to reduce abuse via the intranasal route."	Purdue
PKY182832534	10/2/2000	Sales reps instructed to stress "use as directed" does not lead to abuse. "The idea of less abuse liability due to our controlled release matrix must be properly emphasized for proper pain patients." pg. 1 "In most cases, the abuse issues we hear of are not related to use of OxyContin according to PI." "One of the things he mentioned was his concern that the rep told him there was little or no abuse with OxyContin because of its sustained release matrix." pg. 1 Marketing Expert Team PJM BHM	Purdue

C. Abuse deterrent formulations are safer than non-abuse deterrent formulations.

Bates	Date	Contents	Defendant
JAN-MS-00259893	6/13/2003	"With the added security of abuse deterrence and the flexibility of five dosage strengths" "product that physicians 'trust' to be easy to use and hard to abuse"	Janssen
PKY182832534		"The idea of less abuse liability due to our controlled release matrix must be properly emphasized for proper pain patients."	Purdue
END00125376		"This is a very positive step by the FDA in that it acknowledges the important safety advance that an abuse deterrent	Endo

		formulation offers and prevents easily abusable generics to OxyContin from entering the market."	
END00505817	2013	"Clear that the role of abuse deterrent formulations is impt- has support from FDA saying so, have data that prescript abuse has overtaken street opioid abuse, and puts Opana ER in a very good position."	Endo
ENDO-CHI_LIT-00417068		"Reduces concern and makes it the best choice and easiest to prescribe for the widest array of patients, including those on multiple medications."	Endo

D. Minimize concerns about addictive nature of opioids.

Bates	Date	Contents	Defendant
PPLP003425040	3/19/2014	"The risks of misuse, abuse, and diversion should be considered when prescribing or dispensing OxyContin. However, concerns about abuse, addiction, and diversion should not prevent the proper management of pain."	Purdue
PPLP003291148	11/29/2010	"Remember, concerns about abuse and addiction should not prevent the proper management of pain."	Purdue
PPLP003452443	10/3/2012	"However, concerns about abuse, addiction, and diversion should not prevent the proper management of pain."	Purdue
PPLP003516982		"Misunderstanding of addiction and mislabeling of patients as addicts result in unnecessary withholding of opioid medications. – The American Academy of Pain Medicine and American Pain Society" "A history of substance abuse does not absolutely preclude the use of opioids, but it does warrant extra caution."	Purdue
PPLP003277223		"Misunderstanding of addiction and mislabeling of patients as addicts result in unnecessary withholding of opioid medications. – The American Academy of Pain Medicine and American Pain Society"	Purdue
ALLERGAN_MDL 01610522	7/1/2010	Kadian Learning System (take-home study aid for sales reps) "Concern about abuse, addiction, and diversion should not prevent the proper management of pain."	Allergan

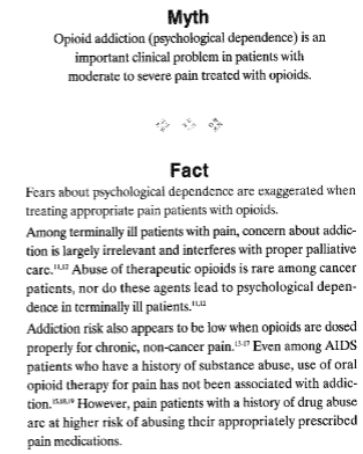
ALLERGAN_MDL_00145639	7/8/11	Oxymorphone Prescribing Information: "Concerns about abuse, misuse, diversion and addiction should not prevent the proper management of pain."	Allergan
Acquired_Actavis_00369188	9/6/2012	Kadian Stocking Offer: "Concerns about abuse, addiction, and diversion, should not, however, prevent the proper management of pain."	Allergan
Acquired _Actavis_00400291	8/1/12	Oxy APAP Prescribing Information: "Concerns about misuse, addiction and diversion should not prevent the proper management of pain."	Allergan
Acquired_ Actavis_01406678	7/12/12	Fentanyl Transdermal System Prescribing Information: "Concerns about misuse, addiction and diversion should not prevent the proper management of pain."	Allergan

E. Science now showing opioids are not as addictive as once thought.

Bates	Date	Contents	Defendant
PPLP004120434	9/20/2006	p. 17 states, "Addiction does not reside solely in drugs - Involves the following factors genetic/familial, environmental, psychiatric, spiritual"	Purdue
PKY180778405	2/2/1995	"Extensive clinical data show that psychological dependence is rare in cancer pain patients without prior history of substance abuse." (p. 58)	Purdue
PKY180266088	6/30/1999	"A survey of over 11,000 patients in a variety of hospitals over several years revealed only four cases of *reasonably well-documented* addiction."	Purdue

F. True patients in pain cannot get addicted – pain protects against addiction.

Bates	Date	Contents	Defendant
END00366720	4/28/2009	"Opioid addiction unlikely to develop. If pain exists then addiction = 1:10,000	Endo
ACTAVIS0006823		"Over time, your body may become tolerant of your current dose. You may require a dose adjustment to get the right amount of pain relief. This is not addiction. It just your body getting used to the drug."	Allergan

PDD1502310593	4/30/1999	Page 5: "It is rare for patients with intractable pain to abuse or divert their prescribed pain medication."	Purdue
ALLERGAN_MDL_01610520	7/1/2010	Kadian Learning System (take-home study aid for sales reps)	Allergan
PURCHI-000674082 PKY181044000	2001	"Addiction risk also appears to be low when opioids are dosed properly for chronic, noncancer pain." – Purdue Professional Sales Aid- Myths about Opioids  **Myth** Opioid addiction (psychological dependence) is an important clinical problem in patients with moderate to severe pain treated with opioids. **Fact** Fears about psychological dependence are exaggerated when treating appropriate pain patients with opioids. Among terminally ill patients with pain, concern about addiction is largely irrelevant and interferes with proper palliative care.[11,12] Abuse of therapeutic opioids is rare among cancer patients, nor do these agents lead to psychological dependence in terminally ill patients.[11,12] Addiction risk also appears to be low when opioids are dosed properly for chronic, non-cancer pain.[13-17] Even among AIDS patients who have a history of substance abuse, use of oral opioid therapy for pain has not been associated with addiction.[15,18,19] However, pain patients with a history of drug abuse are at higher risk of abusing their appropriately prescribed pain medications.	Purdue
JAN-MS-00303825		"According to the Consensus Document reference above, studies indicate that the de novo development of addiction when opioids are used for the relief of pain are low." Janssen Duragesic Press Kit	Janssen
PKY180121679	1999	"Aren't opioid pain medications like OxyContin Tablets 'addicting'? Even my family is concerned about this … Drug addiction means using a drug to get 'high' rather than to relieve pain. You are taking opioid pain medication for medical purposes. The medical purposes are clear and the effects are beneficial, not harmful." – Purdue patient brochure, A Guide to Your New Pain Medicine and How to Become a Partner Against Pain	Purdue

ENDO-CHI_LIT-00024520	2008	**What is the risk of becoming addicted to a long-acting opioid?** Addiction is defined as compulsive drug seeking that is beyond a person's voluntary control even if it may cause harm. Most healthcare providers who treat patients with pain agree that patients treated with prolonged opioid medicines usually do not become addicted.	Endo
ALLERGAN_MDL_0160520	7/1/2010	Kadian Learning System (take-home study aid for sales reps): "It is important to recognize that tolerance and dependence (discussed above) do not indicate addiction. Rather, they are an expected consequence of taking opioids in moderate to high doses for a significant length of time."	Allergan
ENDO-OPIOID_MDL-05654763		"Patients treated with prolonged opioid therapy do not usually develop addictive disorders, though the actual risk is unknown and likely varies with genetic disposition, among other factors. [AAPM, 2001, 2]"	Endo

G. Signs of addiction as simply symptoms of undertreated pain or "pseudoaddiction."

Bates	Date	Contents	Defendant
ALLERGAN_MDL_01610520	7/1/2010	Kadian Learning System (take-home study aid for sales reps): "Pseudoaddiction: Behaviors (that mimic addictive behaviors) exhibited by patients with inadequately treated pain."	Allergan
ALLERGAN_MDL_01610520	pre-7/1/2010	Kadian Learning System (take-home study aid for sales reps): "The problem is even more complex because some patients who are undertreated for their physical pain show the symptoms of "pseudoaddiction." Pseudoaddiction is a set of behaviors (Table 1-3) that are exhibited by patients with inadequately treated pain, including patients with cancer pain. Pseudoaddictive behaviors are not signs of substance abuse, but rater should be considered symptoms of inadequate treatment."	Allergan

Acquired_Actavis_00400291	8/1/12	Oxy APAP Prescribing Information: "Pseudoaddiction refers to pain relief seeking behavior of patients whose pain is poorly managed. It is considered an iatrogenic effect of ineffective pain management. The health care provider must assess continuously the psychological and clinical condition of the pain patient in order to distinguish addiction from pseudoaddiction and thus, be able to treat the pain adequately"	Allergan
Acquired_Actavis_00188875	4/20/11	Oxymorphone HCL Riskmap: …Actavis South Atlantic will stress the requirement for coverage of risk management strategies and would require that education about the following elements be included in all opioid-related educational programs: … -Differentiation among physical dependence, tolerance, pseudoaddiction, and addiction	Allergan
ACTAVIS0006930		"It is important for these audiences to understand the difference between addiction and pseudoaddiction, which involves medication-seeking behaviors solely for the sake of pain relief. While 'tolerance' to opioids can occur, a dose increase of switch to another agent will often yield the needed pain relief. 'Tolerance' can also work advantageously for the patient, since it also applies to adverse events."	Allergan
PPLP003516982		"Pseudoaddiction describes the misinterpretation by members of the health care team of relief-seeking behaviors in a person whose pain is inadequately treated as though they were drug-seeking behaviors as would be common in the setting of abuse."	Purdue
PPLP003862244	8/13/2017	"Patients with pain that is undertreated may do things that, at first glance, look like behaviors of addicts, such as: aggressively demand more medicine, clock watch, doctor shop."	Purdue

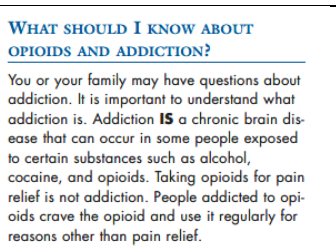
PPLP004120434	9/20/2006	"Pseudoaddiction. Development of relief-seeking behavior as a consequence of inadequate pain management. 3 phases. Inadequate analgesia to manage pain. Escalation of demands for relief with behavioral changes. Crisis of mistrust."	Purdue
PPLPC012000018382		"Pseudo-addiction. This happens to the patient who seek additional medications, appropriately or inappropriately, secondary to significant undertreatment of the pain syndrome. When the pain is treated in the proper manner, this behavior is no longer present." "Pseudo-addiction is a pattern of drug seeking behavior of pain patients who are receiving inadequate pain management that can be mistake for addiction."	Purdue
PKY181150876		"Preoccupation with achieving adequate pain relief can be appropriate behavior in a patient with poor pain control." "Pseudoaddiction – iatrogenic syndrome, behavioral characteristics of addiction, consequence of inadequate pain control, PRN rather than ATC doses, prolonged dose interval, inadequate dose, inappropriate analgesic level."	Purdue
PKY181371853		It is likewise recognized that for patients with continuous pain the use of an as needed (p.r.n) dosing schedule, chronic utilization of drugs with inadequate potency and/or the use of excessive dosing intervals, especially in the inpatient setting, can lead to behavioral symptoms which mimic those seen with psychological dependence. This paper will describe this iatrogenic syndrome as it occurs in medical inpatients and introduce the term 'pseudoaddiction'." -Haddox and Weissman "The pseudoaddiction syndrome is initiated by inadequate pain management." pg. 3	Purdue
PPLP003277223		"Pseudoaddiciton describes the misinterpretation by members of the health care team of relief-seeking behaviors in a person whose pain in inadequately treated as though they were drug-seeking behaviors	Purdue

		as would be common in the setting of abuse."	
JAN00006867		"A related term is pseudoaddiction, which refers to patient behaviors that may occur when pain is under-treated. This includes an increased focus on obtaining medications."	Janssen
PKY181728376		"Pseudoaddiction: Phenomenon characterized by a pattern of drug-seeking behavior due to inadequate pain management; patient mislabeled as an addict. Phenomenon prevented by administration of opioids on a regular basis at doses that provide more 'pain prophylaxis.'" pg. 23	Purdue
PKY180991031		"Misunderstanding addiction may result in unnecessary withholding of opioid medications. Patient maybe mislabeled as an addict – real problem may be that pain is being inadequately treated. Pseudo addiction is a phenomenon characterized by a patient's therapeutic preoccupation with obtaining opioids to achieve a desired level of pain relief. Pseudoaddiction can occur when a patient is prescribed doses that are too low or spaced too far apart to achieve adequate pain relief."	Purdue
PDD1502310593	4/30/1999	Page 4 states: "there is a difference between 'addiction' and 'pain-relief seeking' behavior."	Purdue
JAN-MS-00007119	2008	"[P]seudoaddiction…refers to patient behaviors that may occur when pain is undertreated … Pseudoaddiction is different from true addiction because such behaviors can be resolved with effective pain management." – Let's Talk Pain Website	Janssen
JAN-MS-02268552	1/31/2011	"Patients who watch the clock or know just when the next medication dose is due are likely to be suffering from undertreated pain, not addiction."	Janssen
ENDO-OPIOID_MDL-02472794	1/7/2002	"Pseudoaddiction refers to behaviors suggestive of addiction (eg, multiple prescribes, hoarding) when patients are undertreated for pain."	Endo
JAN-MS-00408610	3/24/2009	"Patients with pain often exhibit behaviors that mimic those of addiction, but the behavior often reflects undertreatment. This is known as pseduoaddiction and is defined	Janssen

		as drug-seeking behavior that imitated the aberrant behavior of true addiction but is actually the result of attempts to alleviate undertreated pain. Adequate pain relief should normalize the behavior of such patients."	
MNK-T1_0001492929		"Pseudoaddiction. Aberrant behaviors due to undertreatment of pain – including inappropriate drug seeking behaviors. Unlike true addiction, when pain is effectively treated – aberrant behaviors resolve, function and quality of life increase."	Mallinckrodt
JAN-MS-00465463	2/9/2012	"Pseudoaddiction superficially resembles addiction but is a direct result of undertreatment of pain."	Janssen
PKY181396701		p. 6 "Pseudoaddiction: 'in the setting of under-treated pain, some patients develop aberrant behaviors that may be quite similar to those associated with addiction. When pain is relieved, the behaviors cease and opioids and other drugs are use responsibly.'"	Purdue
PKY181879304	9/6/2000	"It is imperative that healthcare professionals understand the means of the terms addiction, physical dependence, tolerance, and pseudoaddiction, and that they are able to distinguish the differences between them."	Purdue
PPLPC009000027768		"Pseudoaddiction – a misunderstanding of addiction that may result in unnecessary withholding of opioid medications – patient may be mislabeled as an addict – real problem may be that pain is being inadequately treated."	Purdue
PKY180266088	6/30/1999	"Opioid Myth 1-A: Pseudoaddiction. Iatrogenic Syndrome. Behavioral characteristics of addiction. Obsessive drug-seeking behavior that stops once the pain is relieved, often through an increase in the opioid dose. Consequence of inadequate pain control. Misunderstanding of the phenomenon may lead the clinician to inappropriately stigmatize the patient with the label 'addict'."	Purdue

H. Problems only occur when opioids are abused or used illegally- addicts are bad people who knowingly abused the drugs, not good people who were seeking treatment for legitimate ailments.

Bates	Date	Contents	Defendant
ALLERGAN_MDL 01610520	7/1/2010	Kadian Learning System (take-home study aid for sales reps): "Note that persons who are not themselves opioid abusers but who obtain prescriptions for illicit resale are keenly aware of which clinicians in any area are willing to prescribe medications with a high street value. Often these persons appear to be model patients, answering every question in a manner that will ensure their continued supply. Random drug screens are the most effective tool for detecting such individuals, because an appropriately chosen screening panel will be negative for the opioid that is being prescribed."	Allergan
PPLP003516982		"Identifying patients with drug abuse problems will help you direct them to appropriate care. It also helps ensure that those with legitimate medical need for opioid medications will be able to obtain them." "Addiction is a disease. It is not caused by drugs, it is triggered in a susceptible individual by exposure to drugs, most commonly through abuse."	Purdue
PPLPC012000018382		"Focus on the true pain patient"	Purdue
PPLPC012000018382		"Misunderstanding of addiction and mislabeling patients as addicts results in the unnecessary withholding of opioid medications."	Purdue
PPLP003277223		"Note: Appearance of these indicators serve to alert you to potential problems. They do not mean you should withhold appropriate care."	Purdue
ACTAVIS0006823		"You can become addicted to morphine-based drugs, but it is less likely if you have never had an addiction problem."	Allergan

ENDO-CHI_LIT-00084049	2004	 "Pain relief is an important medical reason to take opioids as prescribed by your doctor. Addicts take opioids for other reasons, such as unbearable emotional problems. Taking opioids as prescribed for pain relief is not addiction."	Endo
PKY181396701		p. 3 "The incidence of addiction was low, and when present most often there was a history of prior drug abuse."	Purdue
PKY181879304	9/6/2000	"The fear of addiction to painkillers hinders therapeutic use of valuable medications, particularly opioids. Addictive behaviors rarely occur in patients who use opuoids for pain relief, especially those with no prior history of substance abuse."	Purdue
PPLPC009000027768		"The trend of increasing medical use of opioid analgesics to treat pain does not appear to contribute to increases in the health consequences of opioid analgeisc abuse."	Purdue
PKY181726711		"Studies indicat that the de novo development of addiciton when opioids are used for the relieft of pain is low."	Purdue

I. If taken as prescribed risk is almost nonexistent.

Bates	Date	Contents	Defendant
ALLERGAN_MDL_01610520	7/1/2010	Kadian Learning System (take-home study aid for sales reps)	Allergan
ALLERGAN _MDL_00405512	7/30/2010	"Proper assessment of the patient, proper prescribing practices, periodic re-evaluation of therapy, and proper dispensing and storage are appropriate measures that help limit abuse of opioid drugs."	Allergan
ABT-MDL-KY-0012834		"It is safe and effective if used properly" pg 11	Purdue
ENDO-CHI_LIT-00551655	11/4/2015	"Opana ER is the single, effective, responsible solution to treat moderate to severe chronic pain, based on true 12 hour efficacy and no CYP450 DDIs, thereby decreasing the worries associated with opioid therapy."	Endo

ACTAVIS0006823		"Morphine and morphine-like-drugs (also called opioids [oh-pee-oyds]) work well for pain and are safe when taken as directed by your healthcare provider."	Allergan
PDD1502310593	4/30/99	"Two opioids with minimal risk for diversion and abuse include OxyContin and MS Contin."	Purdue
JAN00222151	2006	"Addiction is relatively rare when patients take opioids appropriately." – Duragesic website	Janssen
PKY180560092		"When used at appropriate doses to treat pain in selected patients provided with multidisciplinary follow-up, opioids are very unlikely to produce iatrogenic addiction." (p. 20)	Purdue
PKY181879304	9/6/2000	"Truthfully, opioids can be a safe and useful long-term treatment for chronic nonmalignant pain. Patients may be maintained on chronic opioid therapy without developing unmanageable side effects, tolerance, or substance abuse problems."	Purdue
ABT-MDL-KY-0059783 and PPLPC008000016821	 5/8/2001	Pain Action Guide – "Unless you have a history of substance abuse, there is little risk of addiction when these medications are properly prescribed by a doctor and taken as directed." *Pain Action Guide* – American Pain Foundation This is an excellent patient education/aid piece that I previously mentioned to you on e-mail. This currently is available (order code 0P0265) and can be used with all/any of our customers for mass distribution. It can also be used by you to paint the picture of what a patient in pain faces. The more familiar you become with all the materials (especially the slides), the more effective you can become in calming the over-reaction by our customers to the negative media attention and media sensationalism over OxyContin. I would value your input at the upcoming June meetings as to the effectiveness of these materials with your customers. Thank you to all of you for your continued hard work and efforts. I appreciate both immensely. **Remember, we are doing the right thing, and must continue to fight.**	All Purdue

J. Addiction less than 1% or low or rare.

Bates	Date	Contents	Defendant
ALLERGAN_MDL_01610520	7/1/2010	Kadian Learning System (take-home study aid for sales reps)	Allergan
ABT-MDL-KY-0012834		"The National Institute on Drug Abuse has said that most patients using opioids for pain do not become addicted."	Purdue
PPLP003516982		"Physical dependence is a known effect of certain medications." "The number of people who are physically dependent (i.e., at risk for withdrawal syndrome, if the medicines are abruptly stopped) on some type of medication (e.g., antihypertensives, decongestants) far exceeds the number of who are addicted to a drug that induces physical dependence."	Purdue

JAN00222151		"Addiction is relatively rare when patients take opioids appropriately."	Janssen
ENDO-CHI_LIT-00251553		"Most healthcare providers who treat patients with pain agree that patients treated with prolonged opioid medicines usually do not become addicted."	Endo
PKY181150876		"iatrogenic 'addiction' to opioids legitimately used in the management of pain is very rare…"	Purdue
SHC-000026038		"From One Patient to Another-Advice from patients who found relief" "Don't be afraid to take your medication" "Some patients may be afraid of taking opioids because they are perceived as too strong or addictive. But that is far from actual fact. Less than 1% of patients taking opioids actually become addicted." - reference to Porter Jick (at 4)	Purdue
PKY181728376		"Patients may be maintained on chronic opioid therapy without developing unmanageable side effects, tolerance, or substance abuse problems." (p. 9) "Addictive behaviors rarely occur in patients who use opioids under medical care for pain relief, especially those with no prior history of substance abuse." (p. 18) "Addiction rarely seen in patients under medical care with no history of chemical dependence." (p. 64)	Purdue
SHC-000024681		"Drug addiction means using a drug to get 'high' rather than to relieve pain. You are taking the pain medication for medical purposes. The medical purpose is clear and the effects are beneficial, not harmful. True addiction very rarely occurs when opioids are being used properly under medical supervision to relieve pain."(at 4)	Purdue
PKY180991031		"Contradictory to these fears is the finding that the development of addiction is rare in hospitalized patients who received opioid therapy for the treatment of pain . . . Further, tolerance to pain medications does not develop over time. some patients may need higher dosages of a medication to alleviate pain, but these higher dosages do not indicate addiction or diminished effectiveness of the medication."	Purdue
PDD1502310593	4/30/1999	"True addictive behaviors rarely occur in patients who utilize opioids for chronic pain,	Purdue

		especially when the patient has no prior history of substance abuse." (p. 4)	
PKY180989588	2000	"In fact, the rate of addiction amongst pain patients who are treated by doctors is much less than 1%." – Purdue promotional video, featuring Dr. Alan Spanos	Purdue
PKY180555775	3/1/2001	"Iatrogenic addiction to opioids that are legitimately used for the treatment of pain in individuals without a history of substance abuse is very rare."	Purdue
JAN-MS-00653426		"Iatrogenic addiction from opioid analgesia in patients experiencing pain is exquisitely rare."	Janssen
JAN-MS-01192118	9/18/2001	"Iatrogenic addiction following opioid administration is relatively rare. Physicians should not let concerns of physical dependence deter them from using adequate amounts of opioids in the management of severe pain when such use is indicated."	Janssen
JAN-MS-02268552	1/31/2011	"What percentage of patients who receive opioids for short term treatment of acute pain (1-3 days) will become addicted? Less than 1%."	Janssen
ENDO-OPIOID_MDL-02472794		"Addiction to opioids in the context of pain treatment is rare in those with no history of addictive disorders." "The occurrence of addiction as a result of opioid use for pain relief is extremely rare. Several studies have concluded that the risk is far less than 1%."	Endo
ABT-MDL-KY-0059783		Pain Action Guide – "Pain medications rarely cause addiction."	All
PKY180266088	6/30/1999	"addiction is a psychiatric diagnosis that is very rare in caner patients."	Purdue

K. Patients can be easily tapered off opioids.

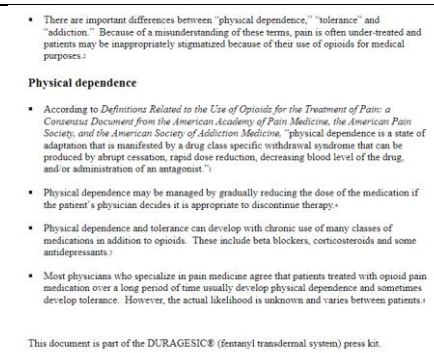
Bates	Date	Contents	Defendant
PPLP003862244	8/13/2017	"These withdrawal symptoms can be avoided by gradually tapering the dosage, as with steroids for arthritis or asthma."	Purdue
JAN00222151		"Physical dependence is not the same as addiction. It may be managed by gradually reducing the dose of the drug if the doctor decides it is appropriate to discontinue therapy."	Janssen
PPLP003277223		"Physically dependent patients can discontinue taking their medicine once their symptoms are	Purdue

		gone by gradually tapering the dosage according to their doctor's orders.	
PKY180990930		"OxyContin 20-60 mg controlled release tablets may usually be stopped abruptly without incident" (pp. 49-50, 57)	Purdue
JAN-MS-00653426		"Opioids can be discontinued in dependent patients without withdrawal difficulties by simply tapering them over about a week."	Janssen
ALLERGAN_MDL_01610520	7/1/2010	Kadian Learning System (take-home study aid for sales reps): "*Development of Tolerance and Physical Dependence* is a major reason some clinicians feel opioid therapy should be limited for patients with CBP. Most clinicians do not consider this a major issue, however. Although tolerance and dependence do occur with long-term use of opioids, many studies have shown that tolerance is limited in most patients with CPC [sic]. Physical dependence simply requires a tapered withdrawal should the opioid medication no longer be needed." "Physical withdrawal generally, but not always, resolves within 5 to 8 days and is not considered life-threatening. Nonetheless, these withdrawal symptoms are uncomfortable and unpleasant, and management of the symptoms is desirable. Medically, treatment of withdrawal symptoms is a straightforward process that can usually be accomplished with minimal difficulty. Detoxification is usually performed by reducing the opioid dosage by 10% to 20% each day, with the entire process requiring 5 to 10 days for completion. Almost any opioid can be used for detoxification because they all have some degree of cross-tolerance."	Allergan
ALLERGAN_MDL_00145639	7/8/11	Oxymorphone Prescribing Information: "When the patient no longer requires therapy with oxymorphone hydrochloride extended-release tablets, gradually taper doses to prevent signs and symptoms of withdrawal in the physically dependent patient."	Allergan
ABT-MDL-KY-0059783		"Physical dependence-which is not to be confused with addiction-occurs in the form of	All

		withdrawal symptoms if you stop taking these medications suddenly. This usually is not a problem if you go off your medications gradually."	
PKY180266088	6/30/1999	"When the pain diminished or is absent, a gradual reduction can be achieved without withdrawal symptoms."	Purdue

L. Dependence is not a significant concern - only physical and easily reversed.

Bates	Date	Contents	Defendant
ABT-MDL-KY-0012834		"Physical dependence and tolerance are normal physiological consequences of extended opioid therapy for pain and should not be considered addiction"	Purdue
PPLP003516982		Physically dependent patients "[c]an discontinue taking their medicine once their symptoms are gone by gradually tapering the dosage according to their doctor's orders" (p. 8)	Purdue
PPLP003549408	1/14/2008	"Do not label a patient addicted if you merely mean physically dependent on or tolerant to opioids" (p. 63)	Purdue
PPLP003862244	8/13/2017	"This means they have developed 'physical dependence' which is merely a side effect of certain medications."	Purdue
JAN00222151		"Physical dependence is not the same as addiction. It may be managed by gradually reducing the dose of the drug if the doctor decides it is appropriate to discontinue therapy."	Janssen
PKY181728376		"Do not label a patient addicted if they are physically dependent on or tolerant to opioids." (p. 8) Physical dependence does not signify addiction (p. 15)	Purdue
PKY180991031		"Do not confuse addiction with physical dependence or tolerance" "Do not label a patient addicted (i.e. psychologically dependent), if you merely mean physically dependent on or tolerant to opioids. Make it clear to patients, families, and staff that tolerance or physical dependence is not the same as addiction."	Purdue
PKY180990930		"Do not confuse addiction with physical dependence or tolerance"	Purdue

		"Do not label a patient addicted (i.e. psychologically dependent), if you merely mean physically dependent on or tolerant to opioids. Make it clear to patients, families, and staff that tolerance or physical dependence is not the same as addiction." (pp. 28-30) fifth vital sign (p. 36) "Contradictory to these fears is the finding that the development of addiction is rare in hospitalized patients who received opioid therapy for the treatment of pain . . . Further, tolerance to pain medications does not develop over time. some patients may need higher dosages of a medication to alleviate pain, but these higher dosages do not indicate addiction or diminished effectiveness of the medication." (p. 47) "Physical dependence is an expected result of opioid use and by itself, does not equate with addiction."	
JAN-MS-00303825		 ▪ There are important differences between "physical dependence," "tolerance" and "addiction." Because of a misunderstanding of these terms, pain is often under-treated and patients may be inappropriately stigmatized because of their use of opioids for medical purposes.1 **Physical dependence** ▪ According to *Definitions Related to the Use of Opioids for the Treatment of Pain: a Consensus Document from the American Academy of Pain Medicine, the American Pain Society, and the American Society of Addiction Medicine*, "physical dependence is a state of adaptation that is manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist."1 ▪ Physical dependence may be managed by gradually reducing the dose of the medication if the patient's physician decides it is appropriate to discontinue therapy.1 ▪ Physical dependence and tolerance can develop with chronic use of many classes of medications in addition to opioids. These include beta blockers, corticosteroids and some antidepressants.1 ▪ Most physicians who specialize in pain medicine agree that patients treated with opioid pain medication over a long period of time usually develop physical dependence and sometimes develop tolerance. However, the actual likelihood is unknown and varies between patients.1 This document is part of the DURAGESIC® (fentanyl transdermal system) press kit.	Janssen
JAN-MS-00456463	9/29/2010	"Dependence is an expected physiological phenomenom when certain drugs are used for sufficiently long periods is neither a necessary nor sufficient defining characteristic of addiction." (one of the authors was manager of regional medical services, Janssen MA) "Phyiscal dependence, like tolerance, has been suggested to be a component of addicton, and the avoidance of withdrawal has been postulated to create behavioral contingencies that reinforce drug-seeking behavior."	Janssen
ALLERGAN_MDL_01610520	7/1/2010	Kadian Learning System (take-home study aid for sales reps):	Allergan

		"It is important to recognize that tolerance and dependence (discussed above) do not indicate addiction. Rather, they are an expected consequence of taking opioids in moderate to high doses for a significant length of time." "*Development of Tolerance and Physical Dependence* is a major reason some clinicians feel opioid therapy should be limited for patients with CBP. Most clinicians do not consider this a major issue, however. Although tolerance and dependence do occur with long-term use of opioids, many studies have shown that tolerance is limited in most patients with CPB [sic]. Physical dependence simply requires a tapered withdrawal should the opioid medication no longer be needed." "Substance dependence is defined as opioid use that is associated with tolerance to the substances' effect or withdrawal symptoms if the substance is discontinued. Care should be taken to differentiate physical withdrawal symptoms from substance craving. Craving is extremely strong psychological desire to use the substance, but is not a physical symptom."	
ALLERGAN_MDL_00145639	7/8/11	Oxymorphone Prescribing Information: "Physical dependence is not the same as drug addiction. Your healthcare provider can tell you more about the difference between physical dependence and drug addiction."	Allergan
Acquired_Actavis_01405682	6/12/13	Morphine Sulfate ER Prescribing Information: "Abuse and addiction are separate and distinct from physical dependence and tolerance. Physicians should be aware that addiction may not be accompanied by concurrent tolerance and symptoms of physical dependence in all addicts. In addition, abuse of opioids can occur in the absence of true addiction."	Allergan
Acquired_Actavis_01406678	7/12/12	Fentanyl Transdermal System Prescribing Information:	Allergan

		"Abuse and addiction are separate and distinct from physical dependence and tolerance. Physicians should be aware that addiction may not be accompanied by concurrent tolerance and symptoms of physical dependence in all addicts. In addition, abuse of opioids can occur in the absence of true addiction and is characterized by misuse for non-medical purposes, often in combination with other psychoactive substances."	
INSYS-MDL-003358164	9/1/11	"Tolerance and physical dependence by themselves do not imply substance dependence or addiction."	Teva
PPLPC009000027768		"Physical dependence is an expected result of opioid use and, by itself, does not equate with addiction." "Addiction has nothing to do with physical dependence."	Purdue

M. Drug abusers and potential addicts can be easily identified and therefore not prescribed opioids, or prescribed opioids and monitored closely.

Bates	Date	Contents	Defendant
ENDO-OPIOID_MDL-02150882	4/7/2006	"Studies have shown that one of the best ways to limit abuse and misuse is to choose appropriate patients for opioid therapy." "Again, proper choice of patient can minimize the likelihood of developing addiction."	Endo
PPLPC012000018382	9/12/2000	"The abuser is a small percentage of patients and it is important to make sure that the true pain patient receives the therapy they deserve."	Purdue
PPLPC012000018382		"Doctor, as you know all opioids have the potential for abuse. OxyContin is a clinically effective opioid and can be a target for individuals who want to abuse the product outside of its intended use. I can provide you with tools to help you properly document the true pain patient and identify the abuser. Re-focus to the true pain patient and then sell."	Purdue
JAN-MS-02328366	1/17/2001	"Although early studies supported the notion that chronic opioid therapy leads to addiction, [ ] more recent data indicate that	Janssen

		this risk is very low in patients with no history of drug abuse." (p. 2)	
ABT-MDL-0000185		"A history of substance abuse dose not absolutely preclude the use of opioids, but it does warrant extra caution."	Purdue
MNK-T1_0001492929		"Reducing the Risk of Misuse and Abuse. Screen Patients, stratify and structure therapy by risk, monitor patients, counsel patients"	Mallinckrodt
ALLERGAN_MDL_01610520	7/1/2010	Kadian Learning System (take-home study aid for sales reps): "Those patients with past histories or strong family histories of substance abuse and psychiatric illness are more likely to suffer from the disease of addiction. Similarly, a social history of personal and familial dysfunction or personality disorder is associated with a high incidence of substance abuse." "Note that persons who are not themselves opioid abusers but who obtain prescriptions for illicit resale are keenly aware of which clinicians in any area are willing to prescribe medications with a high street value. Often these persons appear to be model patients, answering every question in a manner that will ensure their continued supply. Random drug screens are the most effective tool for detecting such individuals, because an appropriately chosen screening panel will be negative for the opioid that is being prescribed." "Consistent signs associated with substance abuse include changes in mental status, recent accidents or trauma, a history of poor impulse control (legal difficulties, gambling, losing jobs), and a history of poor or unpredictable responses to standard pain therapies. Patients with a past history or strong family history of substance abuse (including alcohol abuse) are far more likely to have a substance abuse problem than others are."	Allergan

N. Even patients at high risk of addiction can be safely prescribed opioids by using risk-mitigation strategies such as pain contracts.

Bates	Date	Contents	Defendant
PPLP003291148	11/29/2010	"However, concerns about abuse and addiction should not prevent the proper management of pain." "Purdue Pharma offers the Partners Against Pain Pain Management Kit to aid appropriate pain management."	Purdue
PPLP003461003	9/11/2015	"The potential for these risks should not, however, prevent the proper management of pain in any given patient. Patients at increased risk may be prescribed modified-release opioid formulations such as OxyContin, but use in such patients necessitates intensive counseling about the risks and proper use of OxyContin along with intensive monitoring for signs of addiction, abuse, and misuse."	Purdue
PPLP003277223		"A history of substance abuse does not absolutely preclude the use of opioids, but it does warrant extra caution."	Purdue
MNK_T1-0001492929	7/1/2010	"High-Risk Patients. For patients with a history of drug abuse, psychiatric issues, or serious aberrant drug-related behaviors, consider: frequent and stringent monitoring, consultation with a mental health or addiction specialist."	Mallinckrodt
Acquired_Actavis_00188875	4/20/11	Oxymorphone HCL Riskmap: …Actavis South Atlantic will stress the requirement for coverage of risk management strategies and would require that education about the following elements be included in all opioid-related educational programs: … Identification and ongoing monitoring of patients at higher risk for abuse and diversion, and management tools for pain patients considered for long-term opioid therapy	Allergan

		-Screening tools (e.g. the Screener and Opioid Assessment for Patients with Pain-Revised [SOAPP-R] and the Current Opioid Misuse Measure [COMM]) -Opioid agreement -Plan for follow-up -Role of other modalities such as urine drug screening, pill counts, etc. to assist in monitoring compliance	
PKY181879304	9/6/2000	"Overcoming the Obstacles: Recommendations for Healthcare Professionals. Conduct an addiction history assessment. Develop a controlled substance agreement for the patient to sign. Have good documentation. Assess the patient at each visit for: -pain relief -functioning -side effects –"aberrant drug-related behaviors"	Purdue
PKY181726711	2001	"Furthermore, experience has shown that known addict can benefit from he carefully supervised, judicious use of opioids for the treatment of pain due to cancer, surgery, or recurrent painful illnesses such as sickle cell disease."	Purdue

O. Pain should be treated with opioids.

Bates	Date	Contents	Defendant
PPLP003454006	5/30/14	"The Indications and Usage and Limitations of Use in the FPI do not state that patients must have actually tried or failed both a non-opioid and IR opioid prior to prescribing Butrans or OxyContin." "The new language is intended to reflect that ER/LA opioid analgesics should be prescribed after the prescriber determines that alternative treatment options (eg, non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would otherwise be inadequate."	Purdue
PURCHI-000622986	1/11/1996	"The logical next step for patients no longer responding to or tolerating non-opioids: Add to or replace nonopioid with OxyContin. Q 12 OxyContin – ideal for initial opioid therapy. OxyContin- The one to start with."	Purdue

		"We disagree with the FDA interpretation of the WHO analgesic ladder. Step 2 does not address dosing analgesics on a prn basis. Step 2 relates to adding an opioid to the therapeutic regimen in patients who have persisting pain in the presence of a nonopioid analgesic + an analgesic adjuvant. While we recognize that common medical practice is to treat with non-opioids, then add or change to pm opioids or opioid/non-opioid combination products, and then advance to around-the-clock (a-t-c), this approach is not the best medical practice. This approach can lead to underdosing and episodes of breakthrough pain...While we recognize common medical practice, our goal as a responsible company, is to foster education in the proper use of analgesics"	
PURCHI-000623186	3/8/1996	"In cancer patients: OxyContin may be used as initial opioid therapy for patients no longer responding to or tolerating nonopioids. In non-cancer patients: A prn opioid or OxyContin may be appropriate as initial opioid therapy, as judged by the prescriber."	Purdue
PPLP003997251	12/31/1999	"To establish OxyContin tablets as the opioid of choice in Step 2 of the W.H.O analgesic ladder by positioning it as the opioid to "Start With" for non-cancer pain management."	Purdue
ENDO-CHI_LIT-00417068	09/2012	"Given the benefits it offers, the Opana franchise is the standard of care first-line therapy for the management of pain."	Endo
PDD1502310593	4/30/1999	Effective strategies for cancer pain include: "aggressive use of long-acting, oral opioids as first-line therapy . . . and encouraging the use of short-acting opioids to provide for relief of 'breakthrough' pain." (p. 7)	Purdue
ALLERGAN_MDL_01787026		Co-pay brochure cited in DDMAC Warning Letter: "Why is pain management important? Pain management is a large part of your overall health care plan. Many Americans suffer from chronic or ongoing pain… Managing your pain the right way begins by talking to	Allergan

		your healthcare provider. Discover the cause of your pain by taking note of what makes your pain start and what makes it worse." What is chronic pain? Chronic pain is ongoing and can last longer than 6 months. Chronic pain can be mild or severe…" How can I treat my chronic pain? To help manage your pain, your healthcare provider will determine what level of pain control you need. Depending on what kind of pain you have and how it affects your life, your healthcare provider will choose a drug that works just for you."	
PKY181879304	9/6/2000	"In noncancer patients, a 'prn' opioid or OxyContin may be appropriate as initial opioid therapy, as judged by the prescriber."	Purdue
JAN-MS-00653426	8/1/2001	"Consider as first-line for patients with moderate to severe pain related to cancer or AIDS, or another life threatening illness. Consider for all patients with moderate to severe non-cancer pain, but weigh the influences."	Janssen

P. Undertreated pain should be treated with opioids.

Bates	Date	Contents	Defendant
ENDO-OPIOID_MDL-00585976		"Despite its prevalence, chronic pain is undertreated. Even when patients are prescribed analgesics, pain may persist or worsen due to lack of efficacy. When the initial opioid trial fails, it is important to offer patients a switch in opioid medication in a timely fashion to prevent the development of worsening of chronic pain" "Addition of OPANA ER to the analgesic armamentarium can help address the high incidence and undertreatment of chronic pain"	Endo
ENDO-OPIOID_MDL-02150882	4/7/2006	"Undertreatment of pain produces economic and social costs over tens of billions of dollars each year in the U.S. Opioids have been proven to treat chronic pain effectively and thus can help eliminate undertreatment, if used properly."	Endo

PPLP003516982		"Undertreatment of pain is a serious problem in the United States, including pain among patients with chronic conditions and those who are critically ill or near death. Effective pain management is an integral and important aspect of quality medical care, and pain should be treated aggressively. For many patients, opioid analgesics- when used as recommended by established pain management guidelines- are the most effective way to treat their pain, and often the only treatment option that provides significant relief."	Purdue
PKY181728376		"the undertreatment of pain in today's society is not justified. This joint consensus statement has been produced pursuant to the missions of both organizations, to help foster a practice environment in which opioids may be used appropriately to reduce needless suffering from pain." pg. 38:	Purdue
ACTAVIS0680886		Journal article cited in Kadian Conversion Guide: "Unfortunately, pain is often undertreated and pain management greatly misunderstood."	Allergan
ALLERGAN_MDL_01610520		Kadian Learning System (take-home study aid for sales reps): "Chronic pain is frequently untreated, undertreated, or incorrectly treated." Many patients receive inadequate pain relief because doctors are unwilling to manage chronic pain or do not have sufficient knowledge to treat it properly."	Allergan
PPLP003997190	1996	At PPLP003997205 A stated goal of increasing the number of prescriptions for strong opioids by 10%. States this will be accomplished by convincing health care professionals to use Oxycontin earlier in the patient's treatment cycle. At PPLP003997206 Strategy to convince doctors to start patients on Oxycontin as opposed to lower strength opioids. At PPLP003997206 Oxycontin is the opioid to start with and stay with. "It is anticipated that Kadian will receive a q24h doing	Purdue

		indication, but no less than a q12h approval." "To establish OxyContin as the opioid of choice in Step 2 of the W.H.O analgesic stepladder." "The One to Start With: The logical 'next step' for patients no longer tolerating or responding to nonopioids - conforms to the three-step W.H.O. analgesic ladder" "Patients avoid the added risk of gastric/hepatic/renal toxicity that can occur with products containing aspirin or acetaminophen."	

Q. There is more risk of leaving pain untreated than using opioids to treat pain.

Bates	Date	Contents	Defendant
Acquired_Actavis_00943445		"Chronic Pain is Undertreated. The undertreatment of chronic pain is a serious public health issue that results in enormous social cost and reduces patients' functional status and quality of life."	Allergan
END00366720		"Chronic pain disables more people than cancer or heart disease and cost the American people more than both combined. The annual cost of chronic pain in the US, including healthcare expenses, lost income, and lost productivity is estimated to be $100 million."	Endo
ENDO-OPIOID_MDL-02150882	4/7/2006	"Undertreatment of pain produces economic and social costs over tens of billions of dollars each year in the U.S. Opioids have been proven to treat chronic pain effectively and thus can help eliminate undertreatment, if used properly."	Endo
PURCHI-000706927	1/14/2003	"The undertreatment of pain is a widespread and well-documented health issue in the United States, with the elderly and minority populations at particular risk. The annual cost of chronic pain, including medical expenses, lost income, and lost productivity, is an estimated	Purdue

		$100 billion. Patients with persistent pain are five times more likely than other patients to utilize healthcare services and report impairments of multiple quality-of-life measures, including physical, social, and psychological well being."	
PPLP003549408		"FACT: Pain is Undertreated. All types of pain in all parts of the world are inadequately treated, be it acute or chronic, related to malignant or non-malignant etiologies. Pain can be relieved in up to 90% of cancer patients, yet few there 50% receive adequate treatment. In the US, chronic pain is the most frequent cause of suffering and disability that seriously impairs quality of life."	Purdue
ENDO-CHI_LIT-00417068		"The negative impact of untreated persistent pain on QoL can be significant, disrupting patients' lives and relationships."	Endo
PDD1502310593	4/30/1999	"Pain is one of the most common reasons people consult a physician, yet it frequently is inadequately treated, leading to enormous social cost in the form of lost productivity." (p. 3)	Purdue
PPLP004058784	3/14/2007	"The consequences of untreated or undertreated pain are profound – physically, psychologically, spiritually, as well as economically."	Purdue
ALLERGAN_MDL_01610520	7/1/2010	Kadian Learning System (take-home study aid for sales reps): "Under-treatment of pain results in patients with a very poor quality of life and may lead to feelings of hopelessness and despondency."	Allergan
ALLERGAN_MDL_02233231	5/6/2013	ER/LA Opioid Analgesics REMS website "SCOPE OF THE PROBLEM: According to the 2011 Institute of Medicine Report 'Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research,' as many as 100 million adults in the US report having a common chronic pain condition, exceeding the number affected by heart disease, cancer, and diabetes. The	Allergan

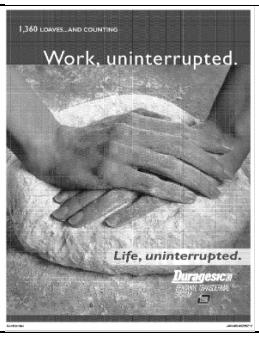
		economic burden of pain to society is staggering. The IOM Report suggests that the annual health economic impact of pain represents a $560 to $645 billion burden to the US (in 2010 dollars)" "At the patient health level, numerous clinical reports suggest chronic pain remains undertreated; the percentage of patients receiving appropriate and adequate treatment has been reported to be as low as 10-25%.	
ABT-MDL-KY-0059783		Pain Action Guide – "If left untreated, chronic pain can prevent you from having a full and meaningful life."	All

R. Opioids offer more effective pain control and are safer than alternatives.

Bates	Date	Contents	Defendant
ALLERGAN_MDL_00001525	02/2013	"Kadian contains morphine as its active ingredient and has a long history of safety and efficacy when used as indicated.'' In response to why should I switch my patients to Kadian objection.	Allergan
ALLERGAN_MDL_0114575		"maintenance therapy with opioids can be safer than the long-term use of other analgesics, such as cyclooxygenase type 2 inhibitors, nonselective nonsteroidal anti-inflammatory drugs, or acetaminophen, in older persons."	Allergan
ENDO-CHI_LIT-00417068	9/2012	"Enables patients to function better throughout the day, sleep well through the night, and achieve the QoL they desire, with minimal cognitive and other side effects." "Reduces concern and makes it the best choice and easiest to prescribe for the widest array of patients, including those on multiple medications."	Endo
PKY181879304	9/6/2000	"Controlled-release Oxycodone Therapy for Patients with Moderate to Severe Osteoarthritis-Related Pain. -Safe and effective."	Purdue

S. Defendants' opioids will make your life better without risk.

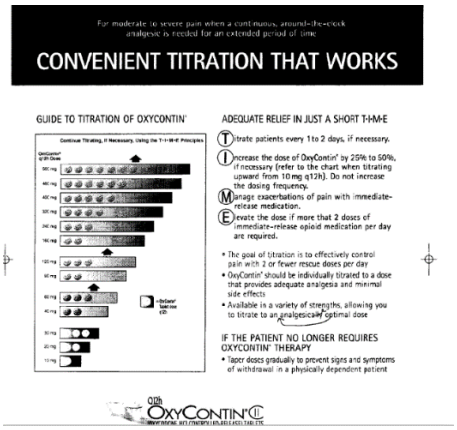
Bates	Date	Contents	Defendant
ENDO-OPIOID_MDL-02150882	4/7/2006	"Multiple studies have confirmed the usefulness of opioids in the treatment of chronic pain and cite the relatively low incidence of abuse and addiction among most patients who receive opioid analgesics. The literature further suggests the potential for increased functioning and improved quality of life significantly outweigh the risk of abuse (American Academy of Pain Medicine, 1997)."	Endo
ENDO-CHI_LIT-00208241		"Opana ER protects me from pain for a full 12 hours so I can go about my daily activities."	Endo
ENDO-CHI_LIT-00417068	9/2012	"Maximum improvement in functionality, consistent pain relief and the best tolerability profile in its class. Enables patients to function better throughout the day, sleep well through the night, and achieve the QoL they desire, with minimal cognitive and other side effects."	Endo
SHC-000024681		"Taking opioids does not mean you are about to die. Many patients take opioids for years to control pain. They will not shorten your life. They will allow you to live with less pain and improve your quality of life."	Purdue
PKY181106858	11/4/1993	"OxyContin will be positioned as the only opioid combining the efficacy and safety of oxycodone with the convenience of a 12 hour dosing schedule, which allows for precise and accurate conversion and titration, while allowing the patient to lead a more normal quality of life." Overall, our strategy for selling OxyContin must focus on the improved quality of life that offers to patients.	Purdue
JAN-MS-00476773	2008	"Myth: Opioids make it harder to function normally. Fact: When used correctly for appropriate conditions, opioids may make it easier for people to live normally." – Janssen patients guide, Finding Relief: Pain Management for Older Adults	Janssen

PDD1501614879			Purdue
JAN-MS-00306286	2003		Janssen
JAN-MS-00299212	2004		Janssen
JAN-MS-00306410		"Game, uninterrupted. Chronic pain relief that supports functionality."	Janssen
JAN-MS-00508566	2006		Janssen
ALLERGAN_MDL_01610520	7/1/2010	Kadian Learning System (take-home study aid for sales reps): "Although the effect of the therapy in reducing the patient's pain is of primary importance, the improvement in the patient's ability to function is considered the gold standard of chronic pain	Allergan

		treatment. Being able to perform more household tasks, walk longer distances, or even return to work are usually considered the key measurements in treating CBP. It is also important to confirm improvement with family members. Too often, a patient reports that their treatment relieves their pain quite effectively, but a spouse complains that the patient is sedated or even intoxicated from their medication. There remains no question that opioids effectively reduce the severity of most types of CBP."	
ABT-MDL-KY-0059783		"Once your pain is under control, your body and mind will be less stressed. You'll be able to sleep better, focus on work, enjoy relationships with family and friends, and take part in social activities." Pain Action Guide	All

T. No maximum dose - if you are in pain more opioids could be given without additional risk (i.e., "titrate to effect" concept from cancer/palliative care should be used with chronic pain).

Bates	Date	Contents	Defendant
JAN00124243	1/22/2013	"Doctor, there is no established ceiling dose for NUCYNTA ER"	Janssen
PPLP003288469	8/19/2016	"The CDC guideline does not limit a clinician's ability to prescribe an opioid dose above 90 MME/day."	Purdue
PPLP003425040	3/19/2014	"Increasing doses of pure mu receptor agonists are associated with increasing analgesia. There is no defined maximum dose; the ceiling to analgesic effectiveness is imposed only by adverse reactions, the more serious of which may include somnolence and respiratory depression."	Purdue
PPLP003343258	8/4/2010	"With pure opioid agonist analgesics, there is no defined maximum dose; the ceiling to analgesic effectiveness is imposed only by side effects, the more serious of which may include somnolence and respiratory depression."	Purdue
PURCHI-000622986	1/11/1996	"No 'ceiling' to analgesic efficacy- may be titrated upward" p. 96	Purdue

		"With full agonists, such as oxycodone, 'effectiveness with increasing doses is not limited by a ceiling.'" p. 74	
PURCHI-000623186	3/8/1996	"With full agonists, such as oxycodone, "effectiveness with increasing doses is not limited by a 'ceiling'."	Purdue
PPLP003996510	8/2/1999	"Help the MD see that 12h is appropriate dosing for the patient controlling the pain, enhancing quality of life, even it if means using an escalating dosage and number of tablets."	Purdue
PKY180704970	11/3/1997	"No maximum daily dose or 'ceiling' to analgesic efficacy – may be titrated upward as necessary."	Purdue
PKY181261176	2002		Purdue
ENDO-CHI_LIT-00084049	2004	"IF I TAKE THE OPIOID NOW, WILL IT WORK LATER WHEN I REALLY NEED IT? Some patients with chronic pain worry about this, but it is not a problem. The dose can be increased or other medicines can be added. You won't 'run out' of pain relief." -- Endo brochure, *Understanding Your Pain: Taking Oral Opioid Analgesics*	Endo
JAN-MS-02268552	1/31/2011	"There is no ceiling or upper limit on how far you can increase doses of opioid medication to improve pain relief."	Janssen
ALLERGAN_MDL_01745342	1/28/11	"KADIAN does not have a ceiling or recommended maximal dose, especially in patients with chronic pain of malignancy. In such cases the total dose of KADIAN should be advanced until the desired	Allergan

		therapeutic endpoint is reached or clinically-significant opioid-related adverse reactions intervene." "KADIAN doses can be titrated up every other day."	
Acquired_Actavis_00943445		No ceiling dose	Allergan
ALLERGAN_MDL 01610520	7/1/2010	Kadian Learning System (take-home study aid for sales reps) "Doses are titrated to pain relief, and so no ceiling can be given as to the recommended maximal dose especially in patients with chronic pain of malignancy. In such cases, the total dose of KADIAN should be advanced until the desired therapeutic endpoint is reached or clinically significant opioid-related adverse reactions occur."	Allergan
PKY180691946	10/20/93	Memo by Mike Innaurato discussing OxyContin - PKY180691948 "Overall, our strategy for selling OxyContin must focus on the improved quality of life that it offers patients." "I feel that the quality of life selling story will be vitally important to the success of OxyContin." "I feel that the quality of life selling story will be vitally important to the success of OxyContin." pg. 3 Marketing Expert Team PJM BHM	Purdue
PKY180266088	6/30/1999	"There is no set of optimal or maximal opioid dose."	Purdue

U. Opioids can be prescribed for any pain condition without risk.

Bates	Date	Contents	Defendant
ENDO-CHI_LIT-00545908	9/22/2006	"So why Opana? Wide range of patients. Opioid experienced and opioid naïve. Acute and chronic pain."	Endo
PPLP003288099	9/1/2016	"Thank you for sharing this with me. (Using page 13 in the CVA) Appropriate	Purdue

		patients for OxyContin may include those not only with cancer pain, but also those with low back pain, and osteoarthritis pain who are experiencing pain severe enough to require daily, ATC, long-term opioid treatment and for whom alternative treatment options are inadequate. For these patients who are on an immediate-release (IR) oxycodone product and whose treatment has proven inadequate, you may consider prescribing OxyContin and evaluate the need for IR oxycodone for breakthrough pain" p.9	
PPLP003461003	9/11/2015	"The indication does not specify any particular chronic pain conditions."	Purdue
PPLP003549408	1/14/2008	"Opioids are the major class of analgesics used in the management of moderate to severe pain because of their effectiveness, ease of titration, and favorable risk-to-benefit ratio." (p. 57)	Purdue
PPLP03997251	12/31/1999	"With the launch of Palladone XL capsules, the promotional focus will be OxyContin Tablets in non-cancer pain." "To establish OxyContin tablets as the opioid of choice in Step 2 of the W.H.O analgesic ladder by positioning it as the opioid to "Start With" for non-cancer pain management." "Enhance the acceptance of opioids for non-cancer pain" "The many benefits of OxyContin Tablets make it logical as the opioid to start with (for patients who would otherwise be started on Percocet, Lortab, Vicodin, Tylenol #3 or Darvocet, W.H.O Step 2) and the opioid therapy to stay with through proper titration as the disease progresses."	Purdue
ENDO-CHI_LIT-00208241		"Good for constant pain no matter the cause"	Endo
ENDO-CHI_Lit-00418075	2/27/2014	"True 12-hour dosing for Veterans and Military Personnel with mild-to-moderate chronic pain."	Endo

ENDO-CHI_LIT-00024587		"All patients with moderate to severe pain, pain-related functional impairment or diminished quality of life due to pain should be considered for opioid therapy."	Endo

V. Opioids can be prescribed to any age group without risk.

Bates	Date	Contents	Defendant
ALLERGAN_MDL_01610520	7/1/2010	Kadian Learning System (take-home study guide for sales reps): "**Special Populations**… Pediatric: Infants under 1 month of age have a prolonged elimination half-life and decreased clearance relative to older infants and pediatric patients. The clearance of morphine and its elimination half-life begin to approach adult values by the second month of life. Pediatric patients old enough to take capsules should have pharmacokinetic parameters similar to adults, dosed on a per kilogram basis."	Allergan
ENDO-CHI_LIT-00024587		"Treatment with opioids is recommended in elderly patients - All patients with moderate to severe pain, pain-related functional impairment or diminished quality of life due to pain should be considered for opioid therapy."	Endo

W. "Round the clock" dosing should be used for chronic pain rather than "as needed" dosing.

Bates	Date	Contents	Defendant
PURCHI-000008094	3/3/2014	"Trying to get the HCP to consider OxyContin instead of oxycodone. Could be taking 4-6 short acting per day, wants him to consider twice daily OxyContin. The patient would be able to reduce the # of short acting they are currently on and only take for break through pain."	Purdue
Acquired_Actavis_00943445		"Longer-acting agents are more effective than short-acting agents for chronic pain; 'around-the-clock' dosing for 'around-the-clock' pain."	Allergan
PPLP003294008	10/26/2011	"OxyContin is an opioid agonist indicated for: Management of moderate to severe pain when a continuous, around-the-clock	Purdue

		opioid analgesic is needed for an extended period of time." p. 5	
PPLP003461003	9/11/2015	"The pediatric trial included opioid tolerant pediatric patients requiring ongoing around-the-clock opioid treatment for the management of moderate to severe malignant or nonmalignant pain."	Purdue
PURCHI-000706927	1/14/2003	"Noting for continuous pain, medications are best given on a time-contingent around-the-clock basis, as drug regimens for the older patient should be simplified as much as possible."	Purdue
PPLP003547645	2/26/2015	"One Hysingla ER tablet taken at the same time each day can provide your patients with around-the-clock hydrocodone delivery."	Purdue
PPLP003549408	1/14/2008	"Give analgesics on a regular schedule to prevent a loss of effectiveness between doses" (p. 58)	Purdue
PPLP003551727	12/1/2009	"Administer analgesics regularly (not only prn) if pain is present most of the day" (p. 59)	Purdue
PPLP003862244	8/13/2017	"Clearly, if you have persistent pain, you would likely prefer to have persistent pain relief, rather than being on a roller-coaster ride with on-again-off-again pain."	Purdue
PPLP004009941	6/24/2013	"Use a regularly scheduled medicine for continuous pain"	Purdue
PDD1502310593	4/30/1999	"Medications for persistent cancer-related pain should be administered on an around-the-clock basis."	Purdue
ALLERGAN_MDL_01610520	7/1/2010	Kadian Learning System (take-home study guide for sales reps) "When patients have constant or nearly constant pain, analgesics should be given "ATC" (around the clock), not "PRN" (when necessary). Fixed, regular dosing intervals are allowed, but frequent episodes of breakthrough pain indicate that regular "around the clock" dosing should be increased."	Allergan

X. "Breakthrough pain" applies to chronic pain, not just cancer pain, and short-acting opioids should be used to supplement long-acting opioids for that reason.

Bates	Date	Contents	Defendant
TEVA_MDL_A_01496786	7/27/2007	"Promote ROO subclass as ideal treatment option for BTP."	Teva
JAN-MS-02387022	8/9/2013	"Moderate to severe acute pain – SAO of choice for appropriate patients such as … on an opioid (CIII) but require additional analgesia."	Janssen
PPLP003288099	9/1/2016	"You ask Dr. Washington how he initiated the patient on Hysingla ER and remind him that the total once daily dose of Hysingla ER should equal what the patient's prior IR hydrocodone total daily dose was. You remind Dr. Washington that other around-the-clock opioid drugs should be discontinued when Hysingla ER therapy is initiated, but you also ask Dr. Washington if he prescribed any IR analgesia for potential breakthrough pain. You also report the adverse events to Purdue Drug Safety Department." p.2 "For these patients who are on an immediate-release (IR) oxycodone product and whose treatment has proven inadequate, you may consider prescribing OxyContin and evaluate the need for IR oxycodone for breakthrough pain. p.9	Purdue
PPLP003549408	1/14/2008	"BREAKTHROUGH PAIN. Transitory exacerbation of pain that occurs on a background of otherwise stable pain in a patient receiving chronic opioid therapy. Supplemental opioid doses are often suggested to manage it when it occurs."	Purdue
PKY180991031		"When breakthrough pain occurs, a "rescue dose" should be administered to the patient. A rescue dose is an opioid with a short half-life and a rapid onset of action that serves as a supplemental or as needed dose that can be offered with a patient's regularly schedule analgesic drug regimen.	Purdue
PDD1502310593	4/30/1999	Effective strategies for cancer pain include: "aggressive use of long-acting, oral opioids as first-line therapy . . . and encouraging the use of short-acting opioids to provide for relief of 'breakthrough' pain." (p. 7)	Purdue

ALLERGAN_MDL_01610520	7/1/2010	Kadian Learning System (take-home study guide for sales reps): "As with cancer pain, opioids for CBP are used 'by the clock' on a scheduled basis, with breakthrough medication sometimes (but not always) made available."	Allergan

138. Defendants also minimized discussion of addiction in sales encounters. For example, in a 2000 training and development meeting devoted to addiction issues, Purdue sales managers were instructed to train their PSRs to avoid talking about addiction issues (i.e., diversion, physical dependence, tolerance, pseudo-tolerance, addiction, pseudoaddiction, abuse) in a selling situation.[280] If these issues arose, PSRs were provided with talking points for refocusing a physician on the "true pain patient," not addiction.[281] With the recognition that patients and prescribers both have concerns over abuse, patient materials attempted to minimize this concern.[282]

139. In addition to downplaying addiction, Defendants' marketing also attacked mainstream thinking about dependence, claiming that patients can easily be tapered off opioids,[283] and that dependence is not a significant concern.[284] Further, Defendants taught prescribers that even patients at high risk of addiction (including drug abusers and addicts) can be treated with

[280] See PKY183146275 at p. 14 ("Manager's Meeting: Handling Abuse, Addiction and Diversion Issues in a Selling Situation").

[281] Id.

[282] See e.g., Living with Chronic Pain, Avinza brochure, END00014041-58. This document was in Endo's production, but it is from King Pharmaceuticals, which manufactured Avinza, and which was subsequently purchased by Pfizer. Avinza was later discontinued by Pfizer after it got approval for Embeda.

[283] PKY181944069 – "A new pain management product that is easy to start and easy to stop!" and 8/10/1999 - PKY180339097 – "Physical dependence is only a problem when opioid medication is decreased or ended abruptly." "When discontinuation is necessary, gradual tapering of opioids will prevent a withdrawal syndrome."

[284] PKY181556552 – "Addiction, physical dependence and tolerance are among the concerns that contribute to the under-treatment of pain with opioid analgesics… physical dependence can be avoided by gradually tapering the dosage, as one would with corticosteroids."

opioids if appropriately monitored.[285] If addiction should occur in patients, Defendants claim that these patients can be easily identified.

140. In addition to the messages above, Defendants' marketing messaging also sought to minimize concerns over addiction, tolerance, and dependence through claims that extended-release and

[285] See e.g., Physicians' Pain Management Speakers Training Program, March 13, 1997, PKY181654983, New Guidelines for the use of Opioids in the Management of Chronic Pain. This document presents numerous messages for the Purdue speakers training program, including for example: "Addiction unlikely in PT without prior history of substance abuse", "pts easily tapered from opioids in MPC's suggests that CPS population without prior hx of drug abuse is distinctly different from street addicts", "Risk of Addiction - studies suggest that inherent predispositions distinguish chronic pain population from addicts (e.g., personality characteristics)", "Addiction studies- conclude that CP patients have low risk of addiction despite chronic opioid usage," "Patients at increased risk may still be appropriately treated with modified-release opioid formulations; however these patients will require intensive monitoring for signs of misuse, abuse, or addiction."; PKY183043997, (A consensus statement from the American Academy of Pain Medicine and the American Pain Society), which states, "Furthermore, experience has shown that known addicts can benefit from the carefully supervised, judicious use of opioids for the treatment of pain due to cancer, surgery, or recurrent painful illnesses such as sickle cell disease." In pharmacy it is understood that this use of opioids may be appropriate in some patients with these conditions. Yet, this document also suggests that "commonly held assumptions [regarding addiction] need modification," including the common "misunderstanding" of addiction and mislabeling of patients as addicts which the authors believe results in unnecessary withholding of opioids, citing "studies indicate that the de novo development of addiction when opioids are used for the relief of pain is low" and challenges respiratory depression, tolerance and diversion.

every 12-hour dosage opioids reduced the risk of addiction while providing around-the-clock analgesia.[286] [287] [288]

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[286] See Table II and Schedule 10.

[287] With respect to the formulations of Duragesic, Janssen sought to differentiate its product claiming its "reservoir" technology was superior to the competition's "matrix" transdermal delivery technology because it was harder to abuse, and had lower "street" value. This was the marketing message until Janssen switched to the same matrix technology in about 2008 and initiated studies to suggest there is not data to support any difference between reservoir and matrix formulations. The economic and marketing reasons to change the Duragesic formulation seemed to outweigh concerns over abuse. Further this example demonstrated that indeed, new formulations were not really different. JAN-0003-0002930, 2004 email chain with subject RE: Johnson & Johnson Achievement Award Nomination; JAN-MS-02410536, 2010 email with subject FW: DURAGESIC – FDA teleconference – meeting summary (70% more residual fentanyl in the matrix patch compared to reservoir; JAN-MS-00280657, 2009 email chain with subject RE:Duragesic – Field voice mail, "I would STRONGLY encourage no proactive communication by the field as I believe it would create a compliance/regulatory issue. I remember if the field mentions DURAGESIC as a CII drug…they have to present an updated PI for compliance and it could lead to what has changed in the PI vs. the old. Plus it could create a question as to our 2004 position on matrix vs. today. A key DURAGESIC prescriber could surface all the issues above."; JAN-MS-02108736, Vorsanger 2006 email with subject RE: Abuse data, "Are there antioxidants in Duragesic? :)", "Very interesting – anyone for tea?".

[288] See also, e.g., MNK-T1_000248919_GL, Managing Pain with Appropriate Use of Opioids, Pocketcard (Magnacet), "Risk of addiction rare," "Single-entity opioids have no maximum dose but may be limited by side effects," "Pseudoaddiction" = "Drug-seeking behavior focused on pain relief, due to undertreatment of pain," and MNK-T1_0002248914_2008, cover email for opioid pocketcard; MNK-T1_0001786865_ASPE Pain v10, Exalgo Pocketcard and MNK-T1_0001786857_2010 Email "ASPE-endorsed Pain PocketGuide and EXALGO opportunity;" see also, similar pocketcards, MNK-T1_0002159712 and MNK-T1_0002159713; MNK-T1_0002183036 and MNK-T1_0002183040; MNK-T1_0001531483 and MNK-T1_0001531484; Note: Mallinckrodt employees who recalled the pocketcards indicated they were distributed to pharmacists and the cards came from the marketing department. New_MNK Deposition pp.201-210 and Williams_MNK Deposition pp.206-207; Mr. Webb testified the pocketcards were "repurposed" for continuing education provided to physicians, nurses pharmacists and others, Webb_MNK Deposition p.54; PKY183225132, "…based on my experience, that long-acting opioid formulations, including OxyContin, have a lower abuse potential that short-acting opioid analgesics."; PDD1501807867, p.4, Sales brochure (Abbott Labs) "A 12h profile is one of the key selling points of Oxycontin. 'Q12h Oxycontin' by definition means that OxyContin's regime only requires two doses, one every 12 hours. "Q12h Oxycontin" in practice means that patients can receive strong, effective analgesia throughout their days and nights. Plus, they receive that strong analgesia with just two doses to remember to take – without the interruptions of a more frequently doses pain management regime"; MNK-T1_0000115442 Email to the Xartemis team and MNK-T1_0000115443, Fingerpaint (3rd party marketing agency) hired by MNK to prepare for launch of Xartemis. Key benefits included, "12-hour dosing", "reduced potential for return of pain," and "[a]buse deterrent qualities that make it more difficult to tamper the product and result in reduced drug high, drug liking, and fewer good drug effects that make the product less desirable for abuse." In the positioning statement, Mallinckrodt asserts that Xartemis XR "provides fast-acting and long-lasting pain relief without concerns about abuse"; E01_00015979, Key Selling Points, abstract of key selling points from the article "Opioid Analgesia an

141. Defendants used this type of messaging to differentiate their newer formulations from older, competing drugs with the same active ingredients. For example, Fentora (fentanyl buccal tablets, transmucosal immediate release fentanyl or "TIRF") was introduced claiming to solve two opioid concerns: (1) the addiction risks of opioids such as OxyContin; and (2) "Breakthrough Pain."[289] Opana (oxymorphone) messages positioned it as a lower-risk, higher-efficacy extended release opioid.[290]

142. Other messages included claims that extended-release drugs had fewer peaks and valleys in absorption and elimination, with less highs and lows, and therefore less chance of addiction and abuse, and that abuse deterrent formulations reduce abuse and are safer than non-deterrent formulations.[291] [292]

Essential Tool in Chronic Pain" by Dr. Neil M. Ellison. The selling points include language that refer to opioids as "not only beneficial but quite safe," "addiction is very rare," "less than 1% of patients become addicted," "[p]hysicians may rely on agents [NSAIDS] they mistakenly perceive to be more benign", "[r]emember that unlike long-term use of opioids, chronic NSAID therapy is associated with end-organ damage," "[t]he key point is that opioids are safe, this can be used to ease a physician's fear of using opioids." Email from Sanjeev Luther, VP Global Business Insights and Forecasting, to the marketing / sales team regarding Xartemis: "The drug is also formulated with abuse deterrent properties including tamper resistance, and the profile is less-liked by recreational drug abusers due to the controlled release, which makes it a potentially less abusable alternative to Percocet and Oxycontin." MNK-T1_0000117111;

[289] TEVA_MDL_A_00730456 (third-party, paid study essentially creating "BTP"); see also TEVA_MDL_A_00369565.

[290] See e.g., ENDO-CHI_LIT-00555142 2007 (OPANA ER Regional Advisory Board NEW YORK Executive Summary); *see also* ENDO-OPIOID_MDL-02489844; JAN-MS-00306327.

[291] See e.g., Kadian 2011 National Sales Meeting, "Putting it all together", 132_ACTAVIS0413281, p.29, "leverage safety profile;" ENDO-CHI_LIT-00190053, ENDO National Advisory Board summary: no drug interactions, true 12-hour dosing, steady plasma levels, durable pain control; Actiq's clear differentiating factor is its rapid onset of analgesia. Actiq 2002 Marketing plan, TEVA_CHI_00042831, p.25; ACTAVIS0335094; ACTAVIS0000564; ACTAVIS0006930; ALLERGAN_MDL_00001525; ALLERGAN_MDL_00072907; ALLERGAN_MDL_00405512; ENDO-CHI_LIT-00550036; MNK-T1_0000115443, 09/30/2013, Fingerpaint; ENDO-CHI_LIT-00553539 (2013) Epidemiologic data on abuse of reformulated OPANA ER will help prescribers understand the value of tamper-resistant formulations; JAN-MS-00259893, (2003) "only AP-48 combines the superior potency of fentanyl with naltrexone in a proprietary formulation to safeguard against unintended usage," "With the added security of abuse deterrence and the flexibility of five dosage strengths," "product that physicians 'trust' to be easy to use and hard to abuse."

[292] Regarding the product feature related to fewer peaks and valleys, it should be noted that while there is a theoretical advantage to this feature I have not seen evidence to support claims that fewer peaks and valleys results in less abuse or better analgesia.

143. Providing a different perspective on addiction and opioid abuse, Mr. Cramer, formerly with Purdue, stated with respect to opioid abuse, *"…an opioid is an opioid is an opioid…."* Suggesting he believes that all opioids have similar potential for harms.[293]

Theme Two: Opioids are effective for, and improve functioning in, patients taking them for long-term and chronic use.

144. In addition to minimizing concerns over addiction, tolerance, dependence, and abuse, Defendants' marketing messages also sought to communicate that for those in pain, opioids can make life better. Communicating messages to Customers like, "there can be life with relief"[294] and "[g]ive your patients the freedom of a life uninterrupted by chronic pain,"[295] Defendants' sought to change the belief (a barrier to opioid use) that using opioids results in a decline in functioning. The Kadian Learning System states: "Although the effect of the therapy in reducing the patient's pain is of primary importance, the improvement in the patient's ability to function is considered the gold standard of chronic pain treatment."[296]

145. This was evidenced in the Opana platform as well, with their tagline of "Opana ER protects me from pain for a full 12 hours so I can go about my daily activities,"[297] and other Opana ER documents stating:

> "Maximum improvement in functionality, consistent pain relief and the best tolerability profile in its class. Enables patients to function better throughout the day, sleep well through the night, and achieve the QoL they desire, with minimal cognitive and other side effects."[298]

A patient guide, Finding Relief: Pain Management for Older Adults, sponsored by PriCara, a division of Janssen, attempted to dispel the "Myth" that opioids make it harder to function

[293] Phil Cramer Deposition, 11-20-18, p.8.
[294] PDD1501614879
[295] JAN-MS-00306286
[296] ALLERGAN_MDL 01610520, Kadian Learning System.
[297] ENDO-OPIOID_MDL-02150882, Module 3, Opana Risk Management Program, 2006 Endo Pharmaceuticals.
[298] ENDO-CHI_LIT-00417068, Opana ER Strategic Platform, Chronic Pain, September 2012.

normally, stating, "Fact: When used correctly for appropriate conditions, opioids may make it easier for people to live normally."[299]

146. As noted in Table II, other messages included, for example:

- Defendants' opioids improve function and will make your life better without risk.[300]
- Opioids have no maximum dose. If you are in pain, more opioids can be given without additional risk ("titrate to effect").[301]
- Opioids can be prescribed for any duration without risk.[302]

147. The book Defeat Chronic Pain Now sponsored by Mallinckrodt's C.A.R.E.S. alliance and used as a sales tool states, *"It is currently recommended that every chronic pain patient suffering from moderate to severe pain be viewed as a potential candidate for opioid therapy."*[303] The book echoes Defendants' core marketing proposition to treat all pain with opioids. In at least some of the opioid marketing, there did not appear to be any boundaries as to who would be targeted

[299] JAN-MS-00476773, Pain Management for Older Adults, Featuring Kathy Baker. Badges from AAPM, AGS, PriCara.

[300] See also, e.g., ENDO-CHI_LIT-00190053, p.46; ENDO-CHI_LIT-00190053, p.56; Actiq 2002 Marketing plan, TEVA_CHI_00042826, p.27; Inventiv Sales training, Actavis overview and Kadian Introduction, ACTAVIS0581557, p.15; "opioid efficacy meets unexpected tolerability" Nucynta training workshop, JAN00102829, p.13; "Living with chronic pain – Your guide to better days and night," (Avinza) "Under proper medical supervision, the risk of opioid addiction is low." END00014041-58; See also, Table II and Schedule 10.

[301] See also, e.g., "Kadian does not have a ceiling or recommended maximal dose" ACTAVIS0361328, p.6; "doctor, there is no established ceiling dose for Nucynta ER." (Note, Janssen did follow this statement here with a recommendation not to exceed 500 mg doses) Nucynta ER Frequently Asked Questions, JAN00124243, p.8; PKY180504210 – "All pure agonist opioids have no maximum daily dose or 'ceiling' on analgesic effect. Thus, opioids can be titrated to as high a dose as clinically necessary to achieve analgesia."; Purdue sales message for Oxycontin sales reps: "With pure opioid agonist analgesics, there is no defined maximum dose: the ceiling to analgesic effectiveness is imposed only by side effects." PKY181686977; See also, Table II and Schedule 10.

[302] See e.g., PKY180425172, "regular use of an opioid medication for pain relief does not stimulate addictive neurobiologic patterns."; PKY180947673, "Many individuals assume that regular use of potentially addictive substances inevitably leads to addiction or drug dependence. THIS IS NOT TRUE! Often such use leads to physical dependence but not necessarily negative consequences or compulsion."; PKY181654983, "Addiction studies conclude that CP patients have low risk of addiction despite chronic opioid usage."; See also, Table II and Schedule 10.

[303] Morellim Arthur_MNL Deposition, pp.380-381; Webb, Kevin_MNK, pp.80-83, 99-100. 107, 133.

with opioid messaging. In a Janssen presentation related to the Imagine the Possibilities Pain Coalition, Janssen lays out plans to reach out to youth, advocating to "[r]each early: elementary school level; via respected channels, e.g., coaches" to deliver a *"practical message"* that *"[p]ain is your body telling you something important."*[304] This presentation also suggests targeting returning veterans and the media to carry the desired opioid messaging: pain must be treated, and treatment with opioids is a good idea.

148. Defendants also focused on using opioids for all types of pain with a rationale that quality of life as a patient outcome is a reason to consider opioid therapy. Some examples include:

- An Opana ER branded slide set on Managing Chronic Osteoarthritis Pain, where elderly patients are targeted for opioid therapy: "All patients with moderate to severe pain, pain-related functional impairment or diminished quality of life due to pain should be considered for opioid therapy."[305]
- An Endo project brief for an Opioid Patient Brochure highlights "Reasons to Believe" and lists "Good for constant pain no matter the cause."[306]
- A reminder for Purdue field sales personnel discussing the pediatric indication for OxyContin states, "The indication does not specify any particular chronic pain conditions."
- Janssen promotes opioid use for any condition with the line "Consider for all patients with moderate to severe non-cancer pain, but weigh the influences."[307]

[304] JAN-MS-02057431, Imagine the Possibilities Pain Coalition, reaching out to youth; Vorsanger_Janssen_Vol.2 Deposition, pp. 673-675.
[305] ENDO-CHI_LIT-00024587, Opana ER For the Management of Chronic Osteoarthritis (OA) Pain.
[306] ENDO-CHI_LIT-00208241, Creative/Project Brief, Project Name: Opioid Patient Brochure.
[307] JAN-MS-00653426 p.19, Chronic Pain: Prevalence and Impact.

Theme Three: Opioid should be first-line therapy for pain.

149. Communicating the message that treating pain patients with opioids first, giving these analgesics preference over other standard pain management regimens, provided Defendants a means to increase overall use of opioids and expand the market for these drugs. Defendants' key marketing messages associated with this theme (Table II and Schedule 10) include messages such as:

- OxyContin, "one to start with, the one to stay with"[308]
- Actiq, "will encourage pure opioid therapy at a much more earlier point in treatment"[309]
- Purdue's messaging to prescribers regarding OxyContin at a meeting of primary care physicians:

> "*Pri-Med represents an important opportunity for the promotion of OxyContin Tablets to an audience of influential primary care physicians from across the area. A primary goal for the Pri-Med meeting is to continue to expand the patient types that are appropriate for OxyContin Tablet therapy. It is important to position OxyContin according to the Package Insert for use in the post-operative patient."*[310]

150. In addition to promoting the need to treat pain, Defendants created a market for "Breakthrough Pain (BTP)." BTP was important in expanding overall demand for opioids because it provided a new Customer need that could be met with Defendants' drugs. It was a key message that could benefit sales of drugs designed to treat BTP or drugs claiming to minimize the occurrence of

[308] See e.g., PPLP003997190, 1996 OxyContin Budget Plan; PPLP003997251, 2000 OxyContin Budget Plan; PURCHI-000622986, Purdue response to promotional questions (Diane Schnitzler, DDMAC).

[309] TEVA_CHI_00042826, p.24, Actiq 2002 Marketing plan.

[310] Selling materials for sales reps, for Primary Medicine (Pri-Med) Today conference, in Ft. Lauderdale, FL, on Marcy 23-25, 2001. PDD1502332817, p.3. In this example, the PI indication of post-operative pain provided an avenue to reach a broader range of patients since post-operative pain is acute pain and routinely treated with immediate release drugs and demonstrates how the PI can be used to leverage utilization.

BTP.[311] In fact, the 2002 marketing plan for Actiq stated that Actiq marketing would center on several goals, including "[e]stablish a solid public relations campaign to begin raising awareness of BTP and ACTIQ among targeted patient populations."[312] BTP was also a prime message utilized to revitalize the marketing of Duragesic (transdermal fentanyl), which by the time of marketing drugs like Opana, was an older agent.[313]

151. Defendants also worked to change existing thinking about opioids as first line therapy for pain by asserting other marketing messages, including:

- Undertreated pain should be treated with opioids.[314]
- There is more risk of leaving pain untreated than using opioids to treat pain.[315]
- Opioids offer more effective pain control and are safer than alternatives.[316]
- Acute pain should be treated with long acting opioids.[317]

[311] See e.g., TEVA_MDL_A_00454816, Actiq Marketing Plan; INSYS-MDL-000445243, Marketing plan for Subsys; MNK-T1_0001048582, Exalgo Marketing Plan; Breakthrough pain Misunderstood, Actiq 2002 Marketing plan, TEVA_CHI_00042826 p.6; Exalgo Account Executive Customer Presentation, slide 6: "EXALGO is a once-daily hydromorphone analgesic that, at steady state, provides consistent 24-hour plasma levels, diminishing high peaks and low throughs." MNK-T1_0002321267; TEVA_MDL_A_01496786, 2008 Pain Care Franchise, 2008 Expense Budget; TEVA_CHOI_00004938, OralVescent Fentanyl, Managed Markets Pre Launch & Launch Plan;

[312] Pyfer Deposition Exhibit 18, 2002 Actiq Marketing Plan, p.5. By this time, Cephalon would now be the third owner of Actiq, previously owned by Abbott and Anesta.

[313] See JAN-MS-02750676 (Duragesic "defend and grow" plan).

[314] See e.g., MNK-T1_000231267 and Table II and Schedule 10.

[315] See e.g., PPLPC019000008891; Mallinckrodt / Covidien presentation titled "Effective Pain Management: Principles of Assessment and Treatment." Slide 4, fourth bullet point: "Undertreatment is the most important obstacle to effective pain control," MNK-T1_0002713527; See also, Table II and Schedule 10.

[316] See e.g., "adverse events similar to placebo over 12 weeks" ENDO-CHI_LIT-00190053, p.42; "modified-release morphine shown safe and effective in treating chronic noncancer pain" CHI_000433744, p.10; Comparison of aspirin, acetaminophen and NSAID safety and efficacy with opioids, noting opioids may be used for acute pain particularly for injuries such as fractures and that long-acting opioids are suggested for treatment of pain that is expected to last longer than 1 week." PKY180141095; "Living with chronic pain – Your guide to better days and night," (Avinza) "Under proper medical supervision, the risk of opioid addiction is low." END00014041-58; See also, Table II and Schedule 10.

[317] PDD8023045826, "principles of titration for around-the-clock pain relief when breakthrough pain occurs more than twice a day." PKY181246683, "This is exactly why patients need oxycontin q12 because

152. As detailed here, in Table II, and in Schedule 10, Defendants' marketing messages were aimed at shifting Customers' thinking regarding the use of opioids for the treatment of pain. This change in the prescribing paradigm included seeking to treat most all pain patients with opioids first. Because Defendants' strategy to shift medical thinking worked, it expanded the total market for opioids.

D. Marketing Messages Over Time

153. As noted in this Report, some of the marketing messages employed by Defendants changed over time, for example, when the OxyContin PI changed in 2006[318], or when part of the marketing focus shifted to tamper-resistance and abuse-deterrence. More recently, Purdue reports that it has stopped marketing opioids entirely.[319] However, marketing principles teach us that the impact of the early marketing, that was so effective in shifting prescribers' paradigms about opioids, would be durable and resistant to change.[320] The aggressive marketing practices employed by Defendants beginning in the mid-1990s created the new opioid paradigm that

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it provides the continuous around the clock. Pain control that they need. Since there's no way to determine which patients will develop Wind Up, It is imperative to treat every patient as if they will."; "Patient Brochure, Living with chronic pain – Your guide to better days and night," from the makers of Avinza ® 24 hour (morphine sulfate extended-release capsules), at END00014047: "Once-a-day medication means you do not have to worry about when to take your next dose." "AVINZA® is the only opioid approved to be dosed not more than once daily. It contains morphine, which has a long history of pain control. When a patient takes AVINZA®, morphine is released gradually over 24 hours. This is why AVINZA® helps people with chronic pain all day and all night. The AVINZA® capsule is designed to keep the amount of morphine in your body steady throughout the day. In clinical studies, AVINZA® gave patients Continuous, reliable pain control over 24 hours with just 1 capsule a day; More active days; More restful nights" END00014041-58; "acute pain doesn't last 4-6 hours- neither should its treatment" Core message email, MNK-T1_0000130448; See also, Table II and Schedule 10.

[318] Mr. Cramer noted in his deposition with respect to OxyContin, "once any reference to the risk of addiction being was removed [from FDA approved labeling], we never referred to it again." (Cramer, Phil 11-20-18 Deposition, p.245.) From a marketing perspective, beliefs, attitudes, and intentions, once created are durable in Customers' minds. Purdue's marketing would be expected to have lasting impact.

[319] Cramer, Phil_11.20.18, p.161.

[320] It is generally understood in marketing that customer beliefs, attitudes, intentions, and values are relatively durable. When considered in relation to products, i.e., beliefs or intentions regarding a product, it is difficult for marketing to create or change them. Hence, once new paradigms are formed, these new beliefs or intentions also become resistant to change. The marketing texts cited earlier in this Report provide extensive insight into this marketing principle.

resulted in blockbuster sales. Marketing principles teach us that two decades of Defendants' marketing aimed at a paradigm shift, will take time and effort to correct.[321]

E. Defendants' Marketing Violated Industry Standards

154. I was asked to assume that the Plaintiffs' expert reports rendered in this case assessed the common messages delivered by the Defendants' marketing and hold the opinions that Defendants' messages were false, misleading, inaccurate, or designed to misstate the risks and benefits of Defendants' drugs. This is consistent with the FDA documents (i.e., warning letters) cited in this Report regarding the false or misleading nature of Defendants' marketing. These opinions are also consistent with the proposition evaluated above that Defendants had a bias toward benefits over harms in their marketing.

155. Further, the use of influencers, KOLs, and professional (advocacy) organizations that Defendants funded and influenced to deliver these messages was more credible because Defendants' hid their influence from the medical community and the public, creating perceptions of unbiased and more scientific information. The marketing analysis in the Report confirms that KOLs and advocacy organizations furthered Defendants' desired promotional messaging in the marketplace. However, Defendants were not forthcoming about their support of these people and activities, or their influence over the conclusions drawn. Defendants' marketing activity supports the proposition that these behaviors were designed to mislead Customers about the impartiality of the messages. In my professional opinion, and considering the full scope of Defendants' marketing, Defendants violated marketing standards by creating and disseminating false or misleading marketing messages that downplayed or minimized the risks associated with opioids, while emphasizing the benefits of their drugs, and by disguising their support of activities aimed at increasing sales of their own products.

[321] Pharmaceutical Marketing, Ch. 2, Rollins, B.L. & Perri, M. (eds.) (2013), p.244.

F. The Defendants' Marketing Was Effective

156. By minimizing concerns over opioid use with these key messages, Defendants' marketing effectively deconstructed the barriers associated with opioids for the treatment of pain. The marketing documents recognized concerns over opioid use, but as a barrier to be overcome through marketing and not as a public health concern.[322] After reviewing numerous marketing documents describing Defendants' marketing planning and execution, spanning more than two decades, it is my opinion that Defendants' approach to marketing opioids was purposeful, aggressive, and effective in increasing sales. The marketing outcomes, including Defendants' own internal metrics, support the fact that the Defendants were able to persuade prescribers and other stakeholders to increase the use of opioids for pain.

157. The impact of marketing efforts can be assessed by examining sales or by how well specific marketing goals were met. Defendants' marketing plans and metrics reveal many such goals and certainly confirm the association between marketing and sales. In the pharmaceutical market, sales are measured through dollar sales figures or by proxy variables such as the numbers of prescriptions written for a drug (TRx), the numbers of "new" prescriptions (NRx), or market share.

158. However, marketing success is relative, as not all products achieve the same levels of utilization. For some products, small increases in TRx or market share can be viewed as success.[323] For example, Endo set a goal for its Opana ER (oxymorphone ER) "To become the #2 branded oral solid CII analgesic..." in recognition that this brand would never overcome oxycodone in market share.[324] Endo's former Senior Director of Marketing, Demir Bingol, agreed that Opana ER was a "successful" franchise that met or exceeded its sales goals.[325] Given this characteristic of the

[322] See e.g., JAN-MS-004078579, "Prevent abuse issues from impacting performance of DURAGESIC". 2002 Duragesic Business Update.

[323] See e.g., 50_MNKT-T1_0000540013, Brands Financial Forecast Review, Exalgo and other product sales Q4 FY1- through Q3 FY13, where Exalgo net sales increase, yet at a decreasing rate.

[324] 2009 Opana Brand Overview, ENDO-CHI-LIT-00022642.

[325] Bingol, Demir_Endo Deposition, pp.39-40.

prescription market, drugs do not have to be blockbusters to be successful.[326] Yet, blockbuster drugs provide insight into how powerful pharmaceutical marketing efforts can be.

159. For example, in its 1995 Launch Plan, Purdue set targets for OxyContin at $25 million in dollar sales and 205,000 prescriptions (TRx) for the drug's first year.[327] Sales surpassed expectations and by 2002, OxyContin sales were targeted to reach $1.2 billion. In 2016, OxyContin sales objectives set targets at $1.442 billion, 4.792M TRx (a seven percent decrease YOY) and a 19.3% share in the extended release opioid market, a decline of just less than one percent.[328] Over a period of more than 20 years, OxyContin went from launch to mature drug status and was able to maintain its market position in spite of the dynamics of the opioid market which was characterized by intense competition and a growing national awareness of the opioid epidemic. This performance, when considered in conjunction with the extensive and detailed marketing plans developed for OxyContin confirms that OxyContin marketing worked to achieve sales of OxyContin.

160. Janssen's Duragesic also demonstrated high year-over-year growth averaging almost 31 percent a year between 1996 and 2002. With sales on track for a yearly total of 692 million in 2002, the company had a vision for 1 billion in sales by 2004 and $2 billion by 2008. These sales figures led Janssen to conclude that Duragesic's product life cycle was still in the growth phase nearly 10 years into its marketing. Most products are in the maturity or decline phases of the product life cycle this far past their introduction.[329] However, due to generic competition, Duragesic sales expectations began to slip after about 2003, but the business plans mapped strategies to continue the brand's success.[330]

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[326] See, e.g., ENDO-OPIOID_MDL-01139611, Endo Commercial Capabilities Overview, J. Goldberg, Managing Director, Corporate Development. This document describes Endo as "the company that Percocet built" and "the company that built Percocet."

[327] PURCHI-003286781, OxyContin Launch Plan, 1995.

[328] PPLPC034001134946, Commercial Organization 2016 Functional Team Objectives (and results).

[329] Duragesic 2002 Business Update, JAN-MS-00478579.

[330] Duragesic Business Update, 2004, JAN-MS-00479441.

Pharmaceutical Marketing Metrics

161. Sales figures are indicators of success in reaching marketing goals and may also be used to monitor corporate goals and even individual (e.g., PSR) performance. Based on established metrics, marketers can assess the overall effectiveness of their marketing, specific advertisements and tactics, or an individual, group, or region by looking at performance over time.[331] For example, strategies and tactics can be tested using common metrics (e.g., TRx, NRx, customer satisfaction) before and after an asset is deployed, messages are communicated, or programs are implemented.[332] [333] Defendants used all these metrics to monitor the impact of their marketing and to adjust their efforts to help ensure that marketing goals were met.[334]

[331] A relevant metric for a sales professional might be the number of prescriptions (TRx) or the number of "new" prescriptions (NRx) stimulated in a geographic area or for a specified time period. See e.g., Coaching & Developing Report, JAN-MS-02991475; ACTAVIS0718729, Dashboard Region A100; ENDO-CHI_LIT-00032434, Opana Brand 2009 Operational Plan.

[332] See generally, the marketing plans cited throughout this Report which contain reference to planned metrics and Schedule 15: Evaluation of Marketing Impact; see also, e.g., PPLPC012000064369, Business Plan written by Bernie Katsur, Purdue National Account Executive; PPLPC015000256864, Marketing report; PPLP003538597, Purdue Butrans Marketing Overview; PPLPC018001107461, pricing analysis; END00716940 p.5, Quarterly Business Review – Opana Franchise; Opana ER Playbook, ENDO-CHI_LIT-00012810; 2009 Opana Brand Plan, ENDO-CHI_LIT-00023298; TEVA_MDL_A_11575042; PPLP003544591, Purdue training slides TEVA_MDL_A_11575560 TIRF; TEVA_MDL_A_11577231, CNS and Pain Care General Business Session (Managers Meeting); TEVA_MDL_A_12517315; TEVA_MDL_A_08714297; 10 Year Plan, PPLPC036000140507; Ipad App, Brand Performance pre-post deployment, Opana Tactical Plan END00717275; PPLPC034001134946, Commercial Organization 2016, Functional Team Objectives; PPLPC029000132250, Sales Force Metrics; PPLPC029000182401, IMS, 2006; Lisa Miller Email with subject: RE: LTC TRx goals for 2016, PPLPC021000829109; MNK-T1_0007810863, Strategy for Growth, FY13 Commercial Scorecard; MNK-T1_0007844237, Exalgo Marketing Plan; JAN-MS-02977249, Nucynta Situation Assessment; NYCZ email with subject: FW: Nucynta Week 7: Monday Milestones, JAN-MS-03015267; INSYS Board of Directors Meeting, INSYS-MDL-007254419; STAT Meeting, Subsys, March 22, 2013, INSYS-MDL-007630138; The Branded Pharmaceutical Strategy, 2012, EPI002481027; Opana Brand Team Scorecard 4/24/2008, EPI002512971; Opana ER Customer Plan, ENDO-OR-CID-01226239; ENDO-CHI_LIT-00035485, sales spreadsheet; Deem_Eshleman_Janssen Deposition, pp.206-214.

[333] See e.g., 16_MNKT-T1_0000124210, Exalgo Business Review, where Mallinckrodt maps graphically the impact of a marketing effort, "Eva" patient profile, TRx change of physicians before and after utilizing a Free Trial Offer; MNK-T1_0000679406, Exalgo Free Trial Offer ROI.

[334] See e.g., Nucynta PhysPulse Wave 1 Summary, JAN00126528 and related PhysPulse docuemtns e.g., JAN00126539, JAN00126250, JAN-MS-00866595, JAN00125893, JAN00126020, JAN00126649, JAN00126932, JAN00126454, JAN00125850, JAN00126691; Jackson, R_Endo Deposition, pp.215-217, 221, 234-235; Adams.John.MNK.1.30.2019 Deposition, pp. 41, 66, 98-99, 121, 162, 349; Barab_Allergan

162. The data provided by marketing research metrics (e.g., deciles, TRx or NRx, product switching, restarting, new prescriptions, refill prescriptions, or location of service such as long-term care, hospital or community, mail order) can be very detailed, for example, breaking down TRx or NRx to the prescriber or zip code level.[335] [336] These metrics are used to benchmark performance and are also useful in identifying potential market growth or opportunities.[337] Indeed, the use of prescriber identifiable data permits manufacturers to precisely monitor and improve the effectiveness of their marketing by evaluating and compensating PSRs based on their individual results.[338]

163. Return on Investment (ROI) is also used to determine the relative value of competing marketing strategies and tactics.[339] However, marketers also use other less quantitative metrics such as "return on objective" or ROO. ROO is best suited to assessing the results of work with, for example, advocacy groups where achievement of an objective is the outcome desired. For example, alliance building, peer-to-peer relationships, customer engagement, and support of

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Deposition, p.219-221; Bearer, Deborah_Teva Deposition, pp. 350-369; Becker, S_MNK Deposition, pp.414-415; Becker.Kevin.MNK.1.24.2019 Deposition, e.g., pp.145, 157, 170; Boothe, Douglas_Allergan Deposition, e.g., pp .48, 140, 148, 166; Boyer, Andrew_Teva Deposition, pp.51-54, 190, 244-251; Burns_Janssen Deposition, pp .219-228; Cramer, Phil 11-20-2019 Deposition, pp. 37-40, 66, 71, 132, 310; Crowley, Jack_Purdue Deposition, pp. 226; Krishnaraj_Insys_30(b)(6) Deposition, pp. 246-263.

[335] See e.g., PPLPC029000182401, IMS, Fueling New Growth Opportunities for the Pharmaceutical Industry, 2006; PPLP004001344; PPLPC019000906695, EOT Update, p.3

[336] Sales Force Metrics, PPLPC029000132250 p.15.

[337] In one assessment of the market landscape (external marketing factors), Purdue noted with a color-coded map, areas in the U.S. with varying levels of "market attractiveness." Based on several variables, it was able to graphically depict areas of opportunity nationwide. Ohio, in RED, was predominately "unattractive" for future growth in the opioid market, with existing high levels of utilization. PPLPC004000374247 p. 9.

[338] Kesselheim AS, Mello MM, Studdert DM. Strategies and practices in off-label marketing of pharmaceuticals: a retrospective analysis of whistleblower complaints. PLoS Medicine 2011;8(4):e1000431.

[339] See e.g., END00717275; PPLPC034001134946 p.7; PPLPC021000800682, p6.; JAN-MS-00313615, ROI Analysis by Territory; JAN-MS-00309600, Strike Force Sales Rep Alignment: Feasibility analysis from ROI Perspective; JAN-MS-00315375, Duragesic Coupon ROI Analysis; END00563922, Opana ER Savings Card Program Promotional Response & ROI Analysis; Burlakoff email, October 31, 2013, INSYS-MDL-000164445, ROI related to speaker programs; Hill email, December 5, 2012, ROI related to speaker programs; Exalgo Free Trial Offer ROI, MNK-T1_0000679406; Promotional Response of Fentora, Findings, TEVA_MDL_A_01543547.

advocacy; while all are marketing activities and important to sales, the success of these activities (e.g., on goodwill, customer loyalty) cannot be fully measured though sales.[340]

164. Based on the metrics I have seen, there is support for the proposition that Defendants' marketing increased the size of the opioid market, effectively expanding sales and increased the use of these dangerous drugs. These efforts and resources devoted to opioid marketing were spent to change prescribers and other stakeholders' perceptions about opioids. There is a clear association between opioid utilization and patient outcomes, including increased analgesia, side effects, diversion, overdose, and death.[341] In my opinion, Defendants who marketed opioids by minimizing the barriers to their use created an expanded demand and substantially contributed to the opioid epidemic.

G. Defendants' Generic Marketing

The Market for Generics

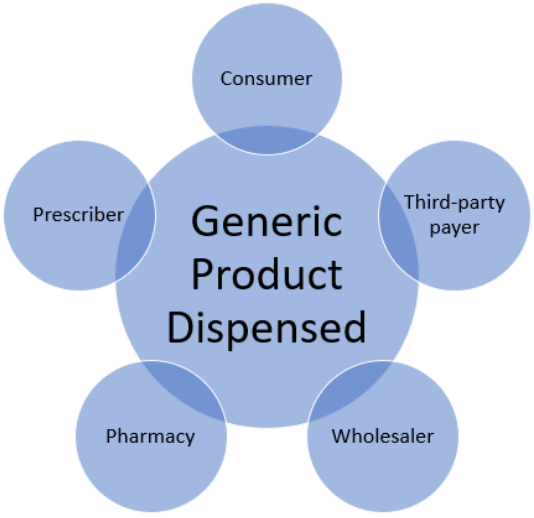
165. Brand name pharmaceutical manufacturers invent and market single-source medication drugs and have exclusive rights to market their patented drugs until patents expire or products are licensed to other companies. The stakeholders in the market for generics are like those for branded drugs. (Figure 3.) Before patent expiration, brand manufacturers extensively advertise and promote their drugs to prescribers, PBMs, TPPs, and others, to increase demand and market share for their products. When manufacturers are effective in creating demand for a drug this benefits the branded medication and creates opportunities for generic entry to the market in the future when the exclusivity granted by the patent expires. Branded advertising prior to generic introduction is both a benefit and threat to generic companies: branded advertising can

[340] See e.g., the "soft" metric of adoption on a third-party formulary, Opana Brand IQ Team Report, ENDO-CHI_LIT-00145643 or "Minutes in front of physician" ENDO-CHI_LIT-00032434, Opana Brand Operational Plan.

[341] See e.g., Hadland S, Rivera—Aguirre A, Marshall B and Cerda M. Association of Pharmaceutical Industry Marketing of Opioid Products with Mortality from Opioid-Related Overdoses. JAMA Network Open. 2019; 2(1)e186007.

expand the market and create loyalty for branded products, making it harder for generics to gain sales once patents have expired.

Figure 3: Generic Market Stakeholders



166. Generics are almost always cheaper than their branded counterparts. The competition that results from generic competitors typically results in prices about 85% less than the brand name drug.[342] Recognizing the potential for cost savings, PBMs, TPPs, and consumers alike have contributed to the extensive use of generics in the U.S. today.

167. Generic manufacturers produce drugs that are chemically identical and bioequivalent[343] (same active ingredient and same processing within the body) to the respective brand-name medication and must meet all FDA and industry manufacturing standards (including all current good manufacturing practices or cGMPs). However, generic manufacturers do not have to conduct safety or efficacy studies needed for the new drug approval process.

[342] www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/genericdrugs/ucm167991.htm (last accessed February 18, 2019).

[343] Pharmaceutical Marketing, Ch. 2, Rollins, B.L. & Perri, M. (eds.) (2013).

168. Generic companies seek markets for medications with higher pre-patent-loss revenues,[344] higher hospital sales, and drugs for chronic diseases because these markets offer high potential for profits.[345] The key variables generic manufacturers consider when deciding to enter a new generic market include consideration of: demand and commercial potential, other market dynamics,[346] technical manufacturing issues,[347] manufacturing costs, supply chain considerations, clinical risk of the drug, competition, the regulatory landscape including any lingering patent (intellectual property) issues such as patent extensions or legal challenges to generic production.[348]

169. The potential for sales, which is to a degree dependent on brand-name sales revenue[349] is typically the primary driver of the "go-no-go" decision to enter a generic market. When considering entering a new market, generic companies must carefully evaluate where resources should be focused and balance multiple inputs to decide to enter a market as opportunities,

[344] Higher sales could be a result of increased advertising spending by brand manufacturers prior to patent loss or due to other characteristics of the drug, such as it being a significant improvement over previous therapy.

[345] Scott-Morton F. Barriers to Entry, Brand Advertising, and Generic Entry in the US Pharmaceutical Industry. International J of Industrial Organization 2000;18:1085-1104; Reiffen D and Ward ME. Generic Drug Industry Dynamics. Review of Economics and Statistics 2005; 87:37-49.

[346] In marketing, careful assessment of the external environment is critical: analyzing, for example, strengths, weaknesses, opportunities and threats, social, legal or regulatory issues. A good example of this is how access to controlled substances is more restrictive than most other drugs, representing a potential limitation in the market which should be considered in the decision to enter a market.

[347] Some medications are technically more difficult to produce and a manufacturer that has special skills with these more difficult drugs might have a competitive advantage over other producers. Quality control considerations may present challenges for medications that are more technically difficult to produce.

[348] A good example of market entry planning and decision making can be seen in the Actavis Pipeline Committee Meeting, October 19, 2011, ACTAVIS0961179, 163 pages, especially at p.2-7, 67-70.

[349] See e.g., Reiffen D and Ward ME. Generic Drug Industry Dynamics. Review of Economics and Statistics 2005;87:37-49; Fiona M Scott Morton. Entry decisions in the generic pharmaceutical industry. RAND Journal of Economics 1999;30(3):421-440; Frank R. G. and D. S. Salkever (1997) "Generic Entry and the Pricing of Pharmaceuticals," Journal of Economics and Management Strategy, Vol. 6, pp. 75–90; Iizuka T. Generic Entry in a Regulated Pharmaceutical Market. Jap Economic Review 2009;60(1):63-81.

challenges, and profits vary significantly between alternatives. The goal of the generic manufacturer is to maximize ROI.[350]

170. Successful companies have a strategic focus, carefully evaluate risks and maximize ROI by carefully managing their product portfolio.[351] [352] These considerations must be optimized because in the generic industry manufacturers do not rely on inventing new products to ensure success. Instead, generic companies leverage their strengths to gain competitive advantages and sell products. A detailed assessment of all these variables is necessary to ensure a good market entry decision and increase the likelihood of success (maximized ROI).

171. In the prescription opioid market, the market for branded drugs expanded quickly making the market attractive for future generic entry. The growth in opioid use, resulting from the marketing efforts of brand-name opioid manufacturers, resulted in higher sales for manufacturers and higher profit potential for generic entrants making the market for opioid analgesics attractive to generic manufacturers.

Generic Pharmaceutical Marketing

172. Pharmaceutical companies who sell generic drugs, like their branded counterparts, are sophisticated in their use of data and knowledge of the prescription market. These companies analyze their own capabilities, supply, and demand for products, and the expectation of profitability upon market entry.

[350] In addition to the ROI, the financial criteria generally used to measure project success include internal rate of return, cash flow, and payback period. See e.g., Actavis, Marketing Department Overview, Allergan-Myers-028, Acquired_Actavis_01367234.

[351] See e.g., Suchak K and Murray LJ. Generic portfolio management: A paradigm for minimizing risk and maximizing value. J of Generic Medicines 2017; 13(2):60-63;

[352] A product portfolio for a pharmaceutical manufacturer is the collection of products (product lines, or brands) that are produced. These products are managed by selecting those with the best strategic fit for the company, optimizing the mix of products to draw on company and market opportunities and to continuously monitor the portfolio for possible changes over time. This process is commonly referred to as portfolio management.

173. For generic medications, the marketing process is different than, but in some cases dependent on, branded drug marketing.[353] Generic manufacturers primarily target pharmacies and wholesale distributors to generate sales but may also target TPPs or PBMs when formulary access is a concern. For generics, the chemical entity selected by the prescriber is usually available from multiple manufacturers who are all competing for market share.[354] While prescribers still choose the medication to use, it is the pharmacy provider, sometimes working in concert with, and subject to the desires of wholesalers, TPPs or PBMs, who typically selects the manufacturer that will supply the generic medication.[355] Consequently, generic pharmaceutical manufacturers focus their promotional marketing efforts on pharmacy providers (e.g., retail-chain pharmacies or mail-order pharmacies) and wholesalers (e.g., McKesson).[356] The key marketing messages are focused on competitive prices and the assurance of a consistent supply of quality generic medications.[357]

174. When a branded manufacturer markets a competing generic for its own brand, it is more difficult to separate branded from unbranded marketing. For example, Kadian was marketed by Actavis as a branded drug, but when competition (Watson) offered a generic morphine sulfate, Actavis responded with its own authorized generic for Kadian. Keeping the Kadian sales team in

[353] Branded drug marketing creates the market for a medication. When patents expire, generic manufacturers take advantage of the opportunities created by brands, prior to generic entry. More aggressive brand advertising can lead to more attractive generic markets.

[354] For example, generic Lipitor® – atorvastatin – might be available from generic manufacturers Ranbaxy, Teva, and Mylan.

[355] The role of the wholesaler in capturing competitive market share is important. Consider promotions like the 1995 Bergen Brusnwig "Glimmer" button on its AccuSource system. This button would show up when a pharmacist sought to purchase a targeted competitor. Pushing the button revealed information on OxyContin to encourage the pharmacist to consider OxyContin instead. (PDD8801142910, Glimmer Button promotion email). This includes marketing services related to pre-launch, which ensure product availability once a drug is marketed. (See e.g., Minutes from the OxyContin Pre-Launch, June 2, 1995; see also, e.g., regarding the wholesale distribution supply chain relationships, National Accounts Memorandum Memo on Wholesaler Development (PKY180256902).)

[356] See e.g., OxyContin Tables NWDA Statement, "Our most important goal was to obtain stocking into the wholesalers and independent pharmacies." PDD1701796415; OxyContin Distribution Plan, September 6, 1995 from G.R. Green, PKY181732400.

[357] See, e.g., Stevenson, George-Endo Deposition pp. 92-96 (explaining generic manufacturers compete based on service levels, fulfillment, and price).

place, Actavis sought to expand the market for Kadian by combining both brand and generic sales for the drug. Generic Kadian by Actavis would be marketed as an alternative to MS Contin and for price sensitive audiences, with marketing messages focusing on its more favorable pricing and availability, and that generic Kadian has the "Same features and benefits as the branded product." While maintaining share of Kadian was important, the goal was to drive sales toward Actavis generic Kadian. This provides insight into how generic and brand marketing are interrelated and difficult to separate.[358]

175. Finally, with respect to this example, the importance of the pharmaceutical supply system can be seen. Wholesaler distributors were integral to selling the generic Kadian since these entities can select the generic manufacturer offering the best pricing and availability to use in their generic source programs and are pivotal in communicating price to pharmacies.

176. As seen with the Kadian example above, some Customers are more sensitive to the price variable of the marketing mix and may defer purchase, or purchase and alternative if the price does not represent a good value for the Customer. This includes patients without prescription insurance, patients with high copayments or deductibles, patients who are in the Medicare "donut hole" and must pay for prescriptions out-of-pocket, and others.[359] For these customers, making a lower priced generic available will increase access because any price barrier is reduced or removed. Therefore, generics work to expand the market by making lower priced alternatives, that patients can more easily afford, available. In addition, lower priced generic drugs are routinely given preferential formulary status (e.g., automatic coverage, preferred tiers, removal of prior authorization requirements) by third party prescription plans and pharmacy benefit managers: reducing insurance coverage barriers to obtaining these drugs and increasing utilization.

[358] Regional Meetings November 2011, Generic Kadian Sales Team Training, ACTAVIS0335094.

[359] "Others" could include, for example, patients who simply wish to pay cash for their prescription opioid and not work through their prescription insurance.

177. Finally, generic companies may increase the supply of opioids in the marketplace through their manufacturing of additional doses of opioids. For example, from about 1999 through about 2015 during which time Defendants requested[360] and were approved to manufacture more opioids.[361]

Defendants' Generic Marketing

178. The Defendants' marketing of brand-name opioids effectively increased the size of the prescription opioid market. This made potential sales of generic opioids more attractive to generic manufacturers considering market entry, some of which also sold brand-name opioids. Generic companies focus on, understanding the market, production (including quality) and manipulating "price," and drug availability to optimize their portfolios and maximize profits.[362]

179. Entry into any generic market is ultimately based on the potential for drug sales and profitability. When considering entry into a generic opioid market, the prototypical "go-no-go" market decision, generic manufacturers considered key factors, such as: [363]

[360] See, Schedule 19: DEA Aggregate Production Quotas containing documents from Mallinckrodt, Allergan, TEVA, PAR, Purdue, Janssen, and Endo related to quota changes.

[361] Schedule 19: DEA Aggregate Production Quotas, 1999-2017.

[362] See e.g., Pipeline Committee Meeting, 29 August 2012, ACTAVIS0395284; Pipeline Committee Meeting, June 20, 2012, ACTAVIS0422012; Pipeline Committee Meeting, October 19, 2011, Oxycodone/Naloxone Project for In-House Development, ACTAVIS0811192; Pipeline Committee Meeting November 23, 2011, ALLERGAN_MDL_00185492; Boothe February 10, 2010 email with subject: RE: DSGP Report as of 2/9/2010 (market decision); Thomson Reuters Street Events, June 12, 2013, Actavis Inc at Goldman Sachs Healthcare Conference, see especially Paul Bisaro, President and CEO commentary on profitability (p.4) and other discussion of company and generic entry. ALLERGAN_MDL_01748522; generic market analysis, rejection decision example, ALLERGAN_MDL_03722181; Actavis Memo, Summary of Required Actions for PAR, ACTAVIS0608086; Sandoz, Quality Agreement on Manufacturing, Packaging and Testing, ACTAVIS0608040; Pharmaceutical R&D Objective Review, September 19, 2000 MNK-T1_000470915; INSYS-MDL-008000496, Ivermectin Topical Cream, Pricing Strategy Assessment, presented to TOPAZ Pharmaceuticals, April 2010; Pharmaceutical R&D Objective Review, September 19th, 2000, "awaiting marketing decision,"MNK-T1_0004709150; TEVA_MDL_A_12517315; TEVA_MDL_A_12644206, S&OP Review.

[363] See e.g., "go" decision in ACTAVIS0911192, Actavis Pipeline Committee Meeting; TEVA_MDL_A_12121906, Demand Planning Analysis Meeting, 2007.

- Awareness of the marketing associated with the branded drugs which increased the demand for these drugs, making the category more attractive from a sales potential. In fact, in some cases generics were being sold to replace a branded drug by the same manufacturer.
- The nature of the drugs, e.g., efficacy, black box warnings, the side effects, their addictive and abuse potential.
- A more complex and therefore more expensive distribution process in the supply chain at the wholesale and retail levels due to the Schedule II, narcotic status.
- The need to continually reevaluate market entry as dynamics (e.g., prices, competition, regulations, market demand, product perceptions) change. This factor is most important after entry when a company decides to stay in each market. This factor certainly suggests that the generic Defendants would have periodically reevaluated all market dynamics, including the national attention focused on abuse, addiction, and death from opioids.

180. Generic marketers thoroughly analyze the market prior to entry to ensure profits and a fit between the company and markets selected for entry. The "go" decision, based on detailed analysis of all salient market entry criteria implies these manufacturers possessed and viewed favorably, information on the market dynamics, positive and negative consequences (e.g., dependence, abuse, diversion and addiction) related to their decisions. The marketing analysis of the go-no-go decision and marketing plans cited in this Report support this proposition.[364]

181. Yet, each generic manufacturer still decided to enter the opioid market based on potential sales and profitability, otherwise the decision would have been "no-go." From a marketing and

[364]Market dynamics related to generic drugs are the subject of news reports. See e.g., Lumpkin and Hancock, February 7, 2019. Trump Administration Salutes Parade of Generic Drug Approvals, But Hundreds Aren't for Sale. https://khn.org/news/trump-administration-salutes-parade-of-generic-drug-approvals-but-hundreds-arent-for-sale/ (last accessed February 9, 2019).

business perspective, for each generic manufacturer who decided to enter opioid market, the profit potential outweighed any barriers or potential negative aspects of market entry, including concerns over the risks of selling opioids. Generic opioid manufacturers entered the market with a focus on harnessing the potential for profits based on high demand for opioids created by the aggressive marketing of brand-name opioids.

182. Finally, generic manufacturers also potentiated the opioid epidemic by providing a lower cost alternative to the more expensive branded opioids. Lower priced opioids meant greater access for most insurance plans since generics are usually covered in preferential tiers, and for cash paying customers. Greater access due to price implies increased use of opioids further expanding the market. This benefit to cash paying patients is also important because cash payments by patients are considered a clue to potential drug abuse and diversion.[365]

H. Wholesale Distributors and Defendants' Marketing

183. The place variable of the 4Ps of the marketing mix identifies the need for products to be efficiently distributed to customers; getting the right products to the right place at the right time.[366] In the pharmaceutical industry, the distribution function is provided by pharmaceutical wholesale distributors, and pharmacy chains who provide all or part of the wholesale distribution function through their own vertically integrated wholesale distribution divisions.[367]

184. In Section II of this Report, the roles of the stakeholders and revenue flows in the integrated supply chain are described. (Figure 4.) As the U.S. drug distribution system currently exists, pharmaceutical manufacturers could not ensure the distribution of their products without both

[365] The level of cash payments for prescription opioids is used by wholesalers and drug enforcement personnel as an indicator of potential abuse. However, cash payments must be considered along with data on employment, insurance coverage, and formulary considerations. When a pharmacy has a high proportion of cash payments for opioids it can spark increased scrutiny or investigation.

[366] Generally, getting the product there at the right price is also necessary, reflecting the interrelatedness of the 4Ps.

[367] Large pharmacy chains who provide wholesale distribution services for their outlets generally also employ a "backup" wholesaler to provide distribution services for medications to ensure product availability.

wholesale distributors and pharmacy providers. Therefore, wholesale distributors and pharmacies are integral to the Defendants' marketing of opioids.

185. The Defendants' marketing messages distributed by the wholesalers focused generally on price, availability, and other features of interest to pharmacy and other buyers.[368] [redacted]

[redacted]

[redacted]

[redacted]

Wholesalers also could include promotional messages in their marketing of manufacturers drugs to prescribers, in addition to the drug availability messages delivered to pharmacies.[370] [371] [372] [373] For example, Actavis targeted the 10,000 top prescribing doctors of Opana ER for a two-wave direct mail and email campaign.[374]

186. Further, unbranded activities were also noted related to generic marketing, such as a 2014 and 2015 Teva unbranded initiative called "Pain Matters" which ran as a documentary on the Discovery Channel, on the internet, and at pain management conferences.[375] Teva's 2015 budget for the Pain Matters campaign was approximately $1 million, and Teva carefully tracked the results.[376] The Pain Matters campaign focused on the use of opioids for chronic pain with

[370] See e.g., CAH_MDL2804_00131705_CONFIDENTIAL, Cardinal Health Marketing Overview where its full scope of marketing services is described, including the eConnection system intended for pharmacists, physicians, and nurses; CAH_MDL2804_02879146, one-page cardinal eConnection document; PPLPC004000083258, Cardinal Health, OxyContin Communication Plan, September 2006; McCormick, Jinping_Allergan Deposition, pp.247-253, 283-284; Allergan_MDL_00684866, John Hansen (Marketing Director at McKesson) with subject: Follow-up discussion re: Actavis oxymorphone campaign (pharmacy awareness).

[371] In 2012, Lisa Robin, Chief Advocacy Officer for the Federation of State Medical Boards proposed distribution of "Responsible Opioid Prescribing: A Clinician's Guide" to physicians in the state of Ohio, through Cardinal Health. Defendants support of the KOL who authored this text (Fishman) and interactions with the Federation of State Medical Boards demonstrates a marketing purpose which in this case clearly focuses on core marketing messages beyond price and product availability. See also, email chain regarding Ohio Prescriber Education Draft Proposal, CAH_MDL2804_00866121; email chain about from Scott Melville of the Healthcare Distribution Management Association expressing interest among his membership (McKesson and Cardinal) in distribution of the Fishman text. PPLP004086826; CAH_MDL2804_00846989, where Responsible Opioid Prescribing is referred to as the result of FSMBs "*Model Policy for the Use of Controlled Substance for the Treatment of Pain"* which was distributed in whole or part by 45 state medical boards. The Fishman book was distributed to nearly 162,000 physicians and other prescribers through accredited CME.

[372] See e.g., Purdue-Seid-059 and Purdue Seid-055 where the McKesson Connect system provides both purchasing and drug information to customers. The information on a new formulation of OxyContin is accessible on this page; PPLPC031001349510, Hysingla ER email communication with link to Pharmacist Guide where there is information on dosing, kinetics, safety information and patient counseling.

[373] A 2001 Purdue National Accounts presentation noted, "Take advantage of educational opportunities" which included educational efforts with major chain pharmacies, trade shows, and Power-Pak® CE programs. (PPLPC008000013580)

[374] Myers, D_Allergan Deposition, Exhibit 15.

[375] Day, Matthew_Teva Deposition, pp.220-228, and Exhibits 23 and 25. (Teva_MDL_A_02296564 & Teva_MDL_A_08657349).

[376] Day, Matthew_Teva Deposition, pp.229-233, and Exhibit 24 (Teva_MDL_A_08657218).

messages such as: "At Teva Pharmaceuticals, we understand that chronic pain affects more than 100 million Americans. . . Prescription opioid medications are an important part of a treatment plan for people living with chronic pain."[377] Teva executives acknowledge that the Pain Matters campaign was a promotional program that was not tied to any of Teva's branded opioids but, instead, was run while Teva was manufacturing and distributing generic opioids.[378]

187. Given the forms of generic marketing, including the essential function of drug distribution in the supply chain system, the increased sales of opioids resulting from Defendants' marketing, could not have occurred without wholesale distributors and pharmacies which completed the supply chain system and made opioids available to patients.

IV. CONCLUSION

188. The aggressive marketing of opioids by Defendants, which included working closely with national level pain advocacy organizations and thought leaders in pain management, resulted in the creation of new medical thinking about pain and its treatment. This new thinking encouraged well-meaning physicians to prescribe more opioids, for more types of pain, sooner and for longer periods of time, without concern for possible harms. Defendants used numerous, time-tested pharmaceutical marketing techniques to target multiple Customers with carefully crafted, well-coordinated messages designed to overcome barriers related to opioid prescribing. Defendants' marketing messages focused on three general themes:

- Addiction, dependence, tolerance, and withdrawal should not be a concern in prescribing opioids.
- Opioids are effective for, and improve functioning in, patients taking them for long-term and chronic use.
- Opioids should be first-line therapy for pain.

[377] Day, Matthew_Teva Deposition Exhibit 26, Pain Matters | Information & Resources for Chronic Pain. This resource also includes information about "Rx Abuse" related to pain.

[378] Morreale, Michael_Teva Deposition, p. 212.

189. Using these general themes, Defendants used a battery of specific marketing messages designed to increase product awareness and systematically remove existing barriers: effectively changing how Customers viewed opioids. Other experts evaluated the nature of these messages and provided the opinions that Defendants' marketing messages were false, misleading, inaccurate, or designed to misstate the risks and benefits of Defendants' drugs. Defendants also downplayed the negative aspects of their products and convinced prescribers, and others, to use opioids sooner in treating pain, at higher doses, and for a broader spectrum of pain types.

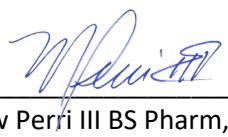
190. Further, Defendants' marketing activities with influencers, KOLs, and professional/advocacy organizations gave their messages more credibility because Defendants hid their funding and influence from the medical community and the public. This created the perception that the information from these marketing efforts was unbiased and more scientific which mislead Customers about the impartiality of the messages.

191. The marketing strategies and tactics Defendants used were effective at gaining market share and expanding the overall market for opioids. This led to a dramatic rise in utilization of opioids in the U.S.

192. Defendants violated marketing standards by creating and disseminating false or misleading marketing messages that downplayed or minimized the risks associated with opioids, while emphasizing the benefits of their drugs, and by disguising their support of activities aimed at increasing sales of their own products.

V. SIGNATURE

193. I reserve the right to amend my opinions in this matter considering any new or additional information.



Matthew Perri III BS Pharm, PhD, RPh

March 25, 2019
Date